Theoretical evidence of a feasible concerted *antara–antara* cycloaddition

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For the first time it is demonstrated, based on theoretical considerations, that concerted *antara–antara* cycloadditions are chemically possible, and even easy to observe for molecules with the appropriate geometry.

Since the discovery of the Diels–Alder reaction in 1928,[1] cycloadditions[2] have become very useful tools in organic synthesis.[3] One of the main features of these reactions is that they frequently follow concerted mechanisms, which accounts for the stereospecificities observed. Many aspects of cycloaddition reactions have been explained by means of the Woodward–Hoffmann rules.[4] According to these rules, two types of reactivity can be considered for each of the reactants involved: *supra* (if newly forming sigma bonds are situated on the same face of the π-system) and *antara* (if these bonds are situated on opposite faces). Since concerted cycloadditions involving more than two reactive systems seem to be very unlikely,[5] cycloadditions can thus be classified as *supra–supra, supra–antara* and *antara–antara*. It is worth mentioning that each of these possibilities would lead to compounds with different stereochemistries.

The *supra–supra* mechanism is involved in most of these reactions, for example Diels–Alder[6] and 1,3-dipolar cycloaddition reactions.[7] On the other hand, the *supra–antara* pathway is much less common[8] and it has recently been disregarded for the ketene + cyclopentadiene reaction,[9] which was, up until then, considered a typical example from theoretical considerations. Theoretical calculations on the ethylene dimerization reaction indicate that the concerted mechanism is not favoured.[10] Finally, to the best of our knowledge, the concerted *antara–antara* cycloaddition mechanism has never been invoked for any chemical reaction to date.

The Woodward–Hoffmann rules predict that *antara–antara* cycloadditions are allowed in the same cases as the *supra–supra* ones, *i.e.* thermal reactions involving $2n + 2$ π electrons and photochemical reactions involving $2n$ π electrons. Competition with the *supra–supra* mechanism could explain the lack of experimental evidence for the occurrence of *antara–antara* cycloadditions, the latter being generally disfavoured because of the molecular distortion necessary to obtain the adequate geometrical requirements in the transition states (TSs). However, the question remains; are concerted *antara–antara* cycloadditions really impossible from an experiment point of view?

In our search for chemical systems for which this kind of mechanism was plausible, we considered the [6 + 4] cycloadditions as a good starting point, given that the combination of triene + diene may offer the flexibility required for an *antara–antara* approach. Thus, the reaction between *cis* hexa-1,3,5-tri-

ene and buta-1,3-diene was chosen as a model example, and, using Density Functional Theory calculations,[11] we were able to build a template for the corresponding *antara–antara* TS. Examination of this structure suggested to us that the simplest way to obtain a chemical system able to give a cycloaddition through a concerted *antara–antara* mechanism would consist of freezing the spatial arrangement of the atoms in the corresponding transition structure. This action would diminish the contribution of the reactive distortion to the activation barrier. With this aim in mind we designed the molecule
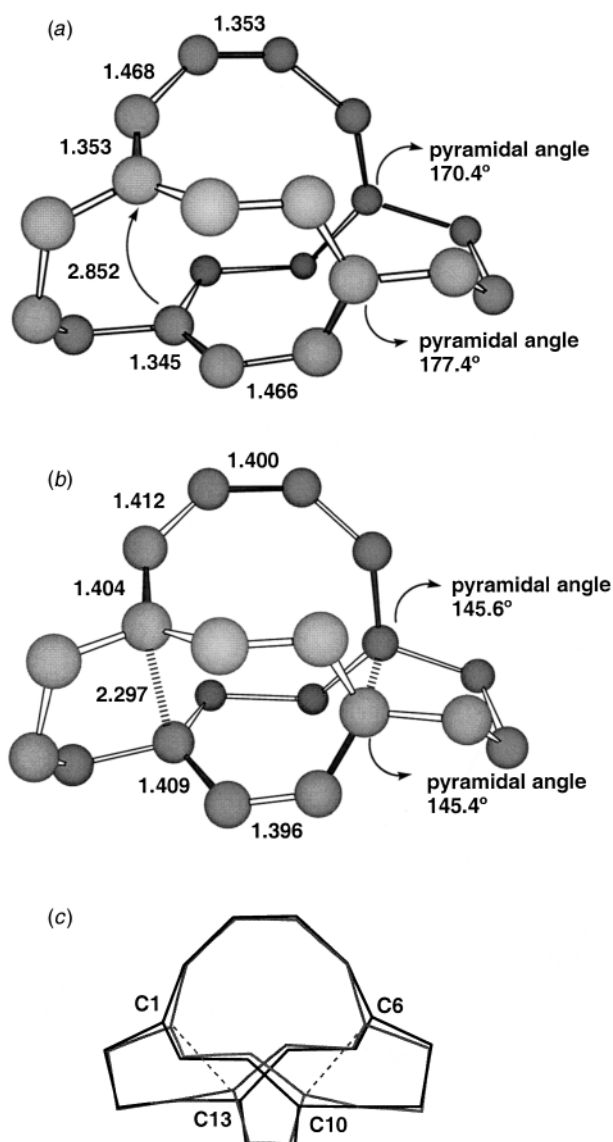
Fig. 1 Some calculated [at the B3LYP/6-31G(d) level] geometrical features of (*a*) antarene and (*b*) the corresponding TS for the *antara–antara* [6 + 4] cycloaddition, and (*c*) a superimposition of the two structures. Hydrogen atoms are omitted for clarity.
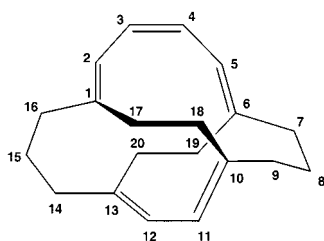
Table 1 Relative energies, enthalpies, free energies and entropies of the structures involved in the *antara–antara* [6 + 4] cycloaddition of antarene, calculated at the HF/6-31G(d) and B3LYP/6-31G(d)[a] theoretical levels

Level	Structures	ΔE_0/kcal mol^{-1}	ΔH_{298}/kcal mol^{-1}	ΔG_{298}/kcal mol^{-1}	ΔS_{298}/cal mol^{-1} K^{-1}
HF/6-31G(d)	Reactant	0.0	0.0	0.0	0.0
	TS	49.7	47.4	48.5	−3.8
	Adduct	−29.0	−27.9	−26.1	−6.2
B3LYP/6-31G(d)	Reactant	0.0	0.0	0.0	—
	TS	16.0	13.7	14.9	—
	Adduct	−23.6	−22.6	−20.7	—

[a] Using the frequencies HF/6-31G(d) for thermochemical data.

(1Z,3Z,5Z,10Z,12Z)-tricyclo[8.6.2.2^{6,13}]icosa-1,3,5,10,12-pentaene, hereafter referred to as 'antarene'.

Fig. 1(*a*) shows some geometrical parameters of this molecule, calculated at the B3LYP/6-31G(d) theory level. As can be seen, antarene consists of the hexatriene and butadiene moieties, linked by two trimethylene and two ethylene bridges in such a manner that the *antara–antara* disposition of the reactive parts of the molecule are strongly enforced. The transition structure of the intramolecular [$_\pi6_a + _\pi4_a$] cycloaddition of antarene could be found at the B3LYP/6-31G(d) level[16] [Fig. 1(*b*)]. This transition structure shows C_2 symmetry, corresponding to a concerted and synchronous process with newly forming bond lengths of 2.297 Å.

Relative energies for the structures involved (Table 1) show that the reaction is exothermic (22.6 kcal mol^{-1}) and presents a low barrier of activation (16.0 kcal mol^{-1}). Since the geometrical constraints of antarene are assumed to make other competitive reactions very difficult, one can deduce that antarene must react through a concerted *antara–antara* cycloaddition mechanism. Fig. 1(*c*) also illustrates this point, showing that the only noticeable geometrical difference between antarene and the transition structure is the displacement of the carbon atoms involved in the formation of the new signma bonds, caused by the change of hybridization from sp^2 to sp^3. As a consequence of the rigidity of the structure, and of the small degree of atomic reorganization along the reaction path, the activation entropy is as low as −3.8 cal mol^{-1} K^{-1}. In fact, the free activation energy is so low (*ca.* 15 kcal mol^{-1}) that one can deduce that antarene should not be very stable in solution at room temperature!

Antara–antara cycloadditions, whose feasibility we have demonstrated for the first time from theoretical considerations, open the door to the synthesis of medium-sized and macropolycycles with unique stereochemical features, and hence to new compounds with different properties.

Notes and references

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