A Theoretical Investigation of the Intermediacy of Alkylidenecarbenes and Isonitriles in the Formation of Furans and Oxazoles

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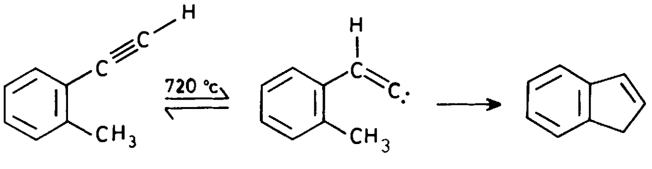
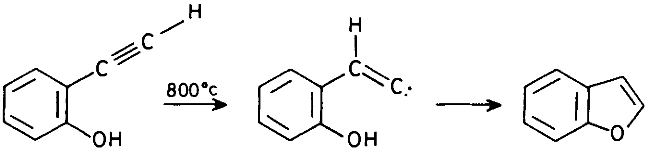
ab initio Calculations on the mechanisms of conversion of 1-ethynyl-2-hydroxyethene (**17a**) to furan (**17e**) and of 1-cyano-2-hydroxyethene (**18a**) to oxazole (**18e**) are reported. Structures of stationary points on the reaction potential surfaces were located at the HF/3-21G level while relative energies were estimated at the MP4SDQ/6-31G* level plus zero-point vibrational corrections. The alkylidenecarbene (**17c**) was found not to be a local minimum whereas the isonitrile (**18c**) was found to be a plausible intermediate during the cyclisation process. The latter lies comfortably in a potential well, making it detectable by spectroscopic means. Again its rearrangement to the cyclic product is rate determining.

In 1974 Brown *et al.*[1] showed using ^{13}C-labelling experiments that arylacetylenes equilibrate with arylvinylidenes. He made use of this to trap the carbene function by an *ortho*-substituent in the flash vacuum pyrolysis of *o*-tolylacetylene (**1**) to give indene (**3**) at 720 °C.



(**1**) (**2**) (**3**)

Bloch and Orvane[2] reported that flash vacuum pyrolysis of 2-ethynylphenol (**4**) at 800 °C results in quantitative formation of benzofuran (**6**), suggesting that the vinylidene (**5**) is formed as an intermediate.

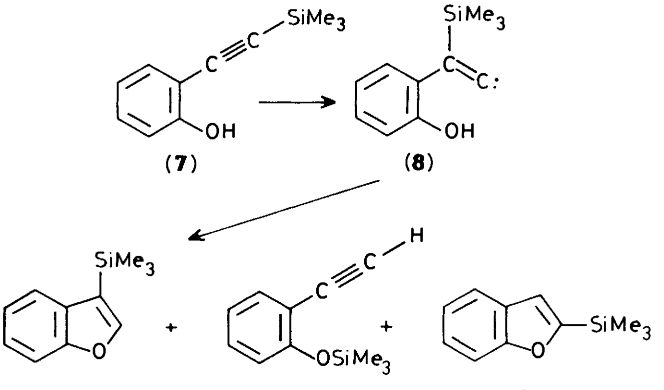


(**4**) (**5**) (**6**)

These reactions involve initially a 1,2-hydrogen shift to form the alkylidenecarbene followed by intramolecular trapping of this carbene function.

Barton and Groh[3] looked at the use of a trimethylsilyl group as the migrating group in (**7**), and found the analogous 3-silylbenzofuran (**9a**) to be a major product. However, it was accompanied by the formation of other products. Of these (**9b**) is thought to have arisen by a second route involving a 1,5-hydrogen migration and a 1,5-silyl shift, while (**9c**) is thought to have been formed from (**9b**) *via* a vinylidene intermediate, which inserts into the Si–O bond.

Subsequently, Karpf and Dreiding[4a] expanded this type of reaction to α-acetylenic ketones (**10**) which are isomerised by flow thermolysis to cyclopent-2-enones (**11**). Again, the carbenes (**10a**) (conjugated with carbonyl groups) were assumed to be intermediates in this 'α-alkynone cyclisation'[4b] [for recent references, see 4(*b*) and 4(*c*)].

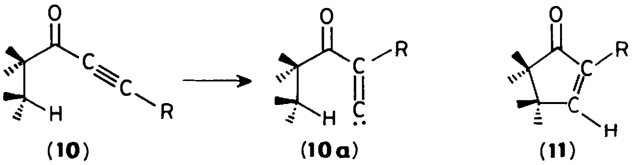


(**7**) (**8**)

(**9a**) (**9b**) (**9c**)

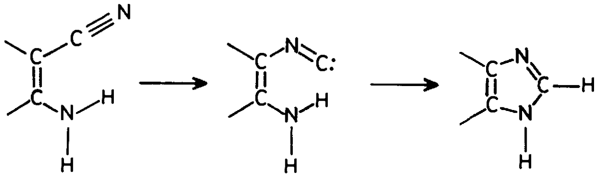
Recent theoretical work on the mechanism of a model α-alkynone cyclisation[5] suggested that the vinylidene (**10a**) can be regarded as a plausible intermediate. In addition, the formation of the cyclic product (**11**) rather than the formation of the vinylidene (**10a**) was found to be the rate-determining step for the overall reaction. However, Karpf[4d] suggested from kinetic studies on this reaction that formation of the carbene was the rate-determining step.

An analogous reaction to the acetylene ⟶ vinylidene ⟶ furan is the reaction involving nitrile ⟶ isonitrile ⟶ oxazole. The photochemical rearrangement of enaminonitriles (**12**) to imidazoles[6] (**13**) is part of a proposed pathway in the prebiological synthesis of purine.[7] Bigot and Roux[8] have studied this isomerisation theoretically. Although the insertion of the isonitrile carbon in (**12a**) into a N–H bond was mentioned this mechanism was not analysed.

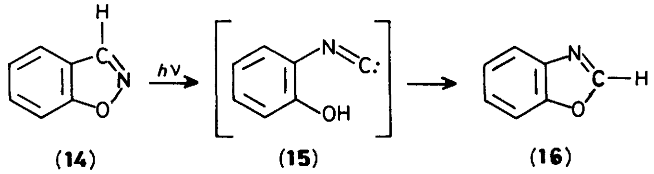


(**10**) (**10a**) (**11**)

Ferris and Antonucci[9] have shown that in the photochemical rearrangement of indoxane (**14**) to benzoxazole (**16**), the



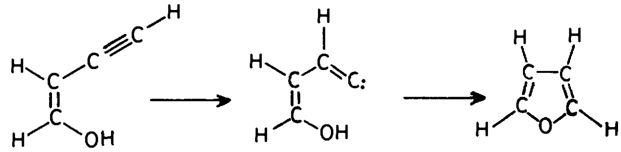
(12) **(12a)** **(13)**



(14) **(15)** **(16)**

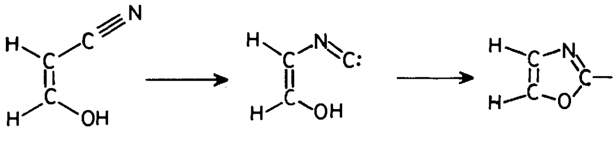
isonitrile (**15**) is assumed to be an intermediate. The reaction possibly involves ring opening of indoxane to form the nitrile, followed by rearrangement to the isonitrile, followed by insertion of this into the O–H bond to form benzoxazole.

As an extension of our theoretical study on the mechanism of these reactions,[5] we set out to determine whether or not the alkylidene-carbene and -isonitrile are plausible intermediates. We have chosen the two reaction pathways to model the transformations being studied (Schemes 1 and 2).



(17a) **(17c)** **(17e)**

Scheme 1.



(18a) **(18c)** **(18e)**

Scheme 2.

Calculations

Molecular geometries of stationary points on the reaction pathways have been optimised at the Hartree–Fock level of theory by the force method with analytical gradient and numerical second derivatives (by gradient finite difference) as implemented in the MONSTERGAUSS program[10] by using the split valence 3-21G[11] basis set. In order to estimate the relative energies between stationary points, we have recalculated single point energies using the Møller–Plesset perturbation theory to second, third, and fourth order[12] with the 6-31G basis and to second order with the 6-31G* basis set. Harmonic vibrational frequencies were calculated at the HF/3-21G level in order to characterise stationary points as minima or transition structures and to calculate the zero-point vibrational contribution to relative energies. These were all calculated using the GAUSSIAN 82 program.[13]

Results and Discussion

(A) *Furan Formation.*— The geometries of the five relevant stationary points (Scheme 1) determined with the 3-21G basis set are displayed in Figure 1. They include three minima, the reactant (acetylene) (**17a**), the intermediate (vinylidene) (**17c**) and the cyclic product (furan) (**17e**), and two transition structures, the 1,2-hydrogen-shift (**17b**) [connecting (**17a**) to (**17c**)] and the 1,5-hydrogen-shift (**17d**) [linking (**17c**) to (**17e**)]. Their total and relative energies calculated at different levels of theory are recorded in Table 1.

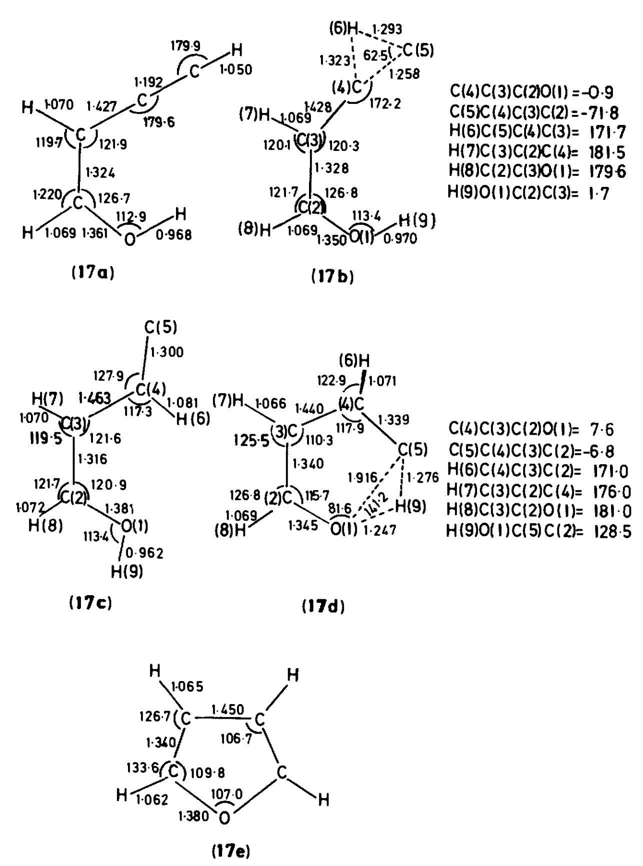


Figure 1. HF/3-21G optimised geometries of stationary points on the acetylene ⟶ furan pathway. Bond lengths are in angstroms and bond angles in degrees.

At the HF/3-21G level, no other minimum could be located for the carbene except for the one shown in (**17c**). All points located with the terminal carbon orientated towards the inner part of the molecule [with the carbene part in a *cis* fashion with respect to C(3)–C(4)] gave one imaginary frequency. The distance between the oxygen and terminal carbon could have been too close if the carbene part was '*cis*'. The minimum obtained could be stabilised by H-bonding, the O(1)–H(6) distance is 2.102 Å. Because the carbene stationary point located was more stable with H(9) orientated in the position shown in (**17c**), a stationary point for the acetylene with a similar orientation for this hydrogen was located. However this was found to be 5.7 kcal mol^{-1} (3-21G) less stable than (**17a**).

The overall reaction is exothermic to the extent of −39.7 kcal mol^{-1} (Table 1). At the MP4/6-31G level, the carbene (**17c**) lies in a flat potential well (Figure 2). However, it turns out to be higher in energy than (**17b**) following incorporation of polarisation d-functions into the wavefunctions. In other words, the carbene structure is probably not a local minimum on a correlated potential-energy surface using an appropriately large basis set. Thus the conversion of the acetylene (**17a**) into the cyclic product (**17e**) occurs in an elementary step involving only one transition structure. However full geometry optimization of such a transition structure can only be confirmed at higher levels of theory (at least MP2/6-31G*), which is beyond our present computational resources.

Table 1. Total (au), relative (kcal mol^{-1} in parentheses), and zero-point vibrational (Z.P.E.) (kcal mol^{-1}) energies of stationary points (**17a–e**) using HF/3-21G geometries.

Species	(**17a**)	(**17b**)	(**17c**)	(**17d**)	(**17e**)
HF/3-21G	−227.302 18 (0.0)	−227.206 43 (60.1)	−227.227 75 (46.7)	−227.188 60 (71.3)	−227.350 08 (−30.1)
HF/6-31G	−228.481 96 (0.0)	−228.387 76 (59.1)	−228.412 10 (43.8)	−228.364 80 (73.5)	−228.525 32 (−27.2)
HF/6-31G*	−228.567 95 (0.0)	−228.493 14 (46.9)	−228.499 58 (42.9)	−228.450 66 (73.6)	−228.622 69 (−34.3)
MP2/6-31G	−228.950 02 (0.0)	−228.850 21 (62.6)	−228.854 08 (60.2)	−228.851 14 (62.0)	−228.994 15 (−27.7)
MP3/6-31G	−228.960 32 (0.0)	−228.862 58 (61.3)	−228.876 58 (52.5)	−228.855 23 (65.9)	−229.006 73 (−29.1)
MP4SDQ/6-31G	−228.976 81 (0.0)	−228.879 40 (61.1)	−228.892 48 (52.9)	−228.877 63 (62.2)	−229.021 09 (−27.8)
MP2/6-31G*	−229.241 45 (0.0)	−229.160 97 (50.5)	−229.148 30 (58.4)	−229.152 73 (55.7)	−229.307 47 (−41.4)
NIF[a]	0	1	0	1	0
ZPE[a]	41.0	37.0	39.0	37.4	42.8
MP4SDQ/6-31G*[b]	(0.0)	(49.0)	(51.2)	(55.9)	(−41.5)
Estimated[c]	(0.0)	(45.0)	(49.2)	(52.3)	(−39.7)

[a] Number of imaginary frequencies and zero-point energy (scaled by 0.9) at HF/3-21G. [b] Estimated using the additivity approximation: ΔE(MP4/6-31G*) = ΔE(MP4/6-31G) + ΔE(MP2/6-31G*) − ΔE(MP2/6-31G). [c] Including ΔE(MP4/6-31G*) and ZPEs.

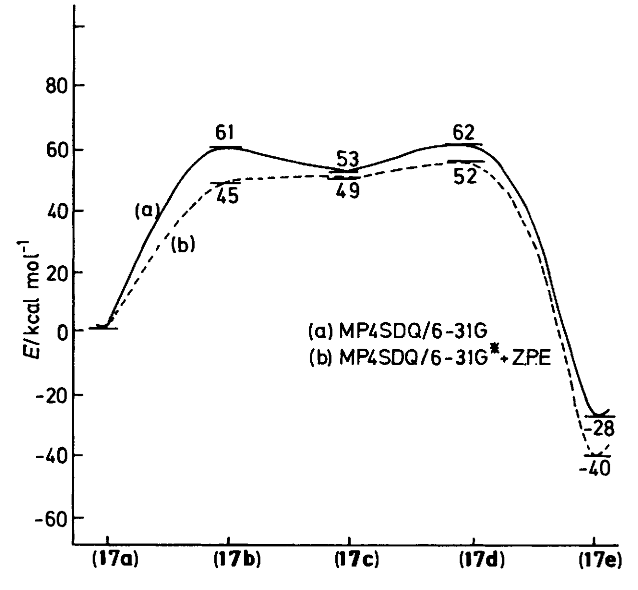


Figure 2. Schematic energy diagram for the acetylene ⟶ furan transformation. Energies are given in kcal mol^{-1}.

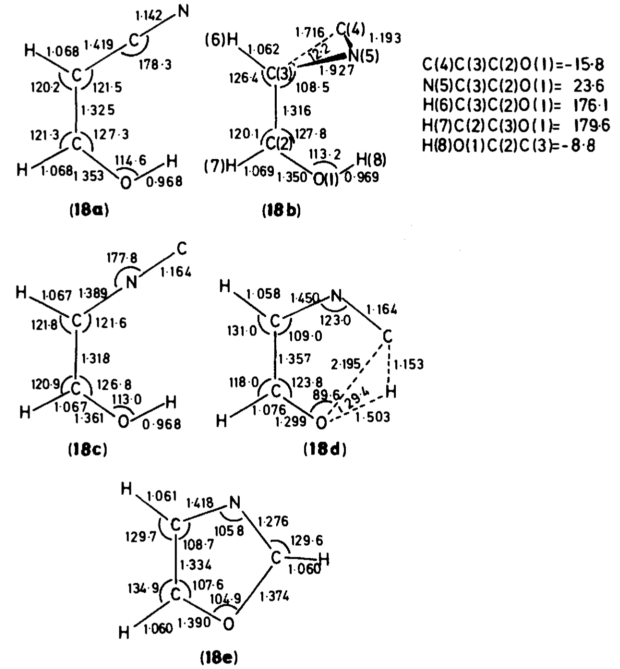


Figure 3. HF/3-31G optimised geometries of stationary points on the nitrile ⟶ oxazole pathway. Bond lengths are in angstroms and bond angles in degrees.

In summary, our preliminary calculations suggest that alkylidenecarbene (**17c**) is not a discrete intermediate during the transformation of acetylene (**17a**) to furan (**17e**). This is in contrast to the α-alkynone cyclisation[4,5] mentioned above. Thus, the carbene formation might at best, be present in the transition structure connecting (**17a**) to (**17e**). Fusion of the system to a benzene ring such as in (**1**) and (**4**) might stabilise the carbenes somewhat but it is not certain whether the latter could become local minima on the potential-energy surfaces.

(B) *Oxazole Formation*.—The geometries of the five relevant stationary points determined with the 3-21G basis set are displayed in Figure 3. They include three minima, the reactant (nitrile) (**18a**), the intermediate (isonitrile) (**18c**), and the cyclic product (oxazole) (**18e**), and two transition structures, the 1,2-hydrogen-shift transition (**18b**) [connecting (**18a**) to (**18c**)] and the 1,5-hydrogen shift (**18d**) [linking (**18c**) to (**18e**)]. Their total and relative energies calculated at different levels of theory are recorded in Table 2.

The nitrile to isonitrile rearrangement takes place by the formation of a bridged-type transition structure (**18b**), with both C(3)–C(4) and C(3)–N(5) bonds being quite long. C(4) is pushed below the plane by 15.8° while N(5) is raised out of the plane by 23.6°.

The isonitrile structure (**18c**) is found to have a quasi-linear C–N–C arrangement. Attempts to locate a minimum with a CNC angle of *ca.* 120° failed, with the geometry converging to the linear arrangement.

The planar transition structure for cyclisation (**18d**) having an O–H distance of 1.503 Å and C–H bond length of 1.153 Å

Table 2. Total (au) relative (kcal mol^{-1} in parentheses), and zero-point vibrational (ZPE) (kcal mol^{-1}) energies of stationary points (**18a–e**) using HF/3-21G geometries.

Species	(**18a**)	(**18b**)	(**18c**)	(**18d**)	(**18e**)
HF/3-21G	−243.266 35	−243.139 82	−243.233 05	−243.126 78	−243.251 05
	(0.0)	(79.4)	(20.9)	(87.6)	(9.6)
HF/6-31G	−244.519 87	−244.395 58	−244.488 31	−244.379 19	−244.502 51
	(0.0)	(78.0)	(19.8)	(88.3)	(10.9)
HF/6-31G*	−244.628 59	−244.522 49	−244.594 82	−244.487 59	−244.628 66
	(0.0)	(66.6)	(21.2)	(88.5)	(−0.04)
MP2/6-31G	−245.013 35	−244.892 55	−244.965 69	−244.903 71	−244.996 52
	(0.0)	(75.8)	(29.9)	(68.8)	(10.6)
MP3/6-31G	−245.010 07	−244.892 17	−244.969 27	−244.888 37	−244.999 61
	(0.0)	(74.0)	(25.6)	(76.4)	(6.6)
MP4SDQ/6-31G	−245.030 21	−244.913 02	−244.989 84	−244.917 94	−245.016 10
	(0.0)	(73.5)	(25.3)	(70.4)	(8.9)
MP2/6-31G*	−245.332 76	−245.227 02	−245.289 18	−245.227 99	−245.345 67
	(0.0)	(66.4)	(27.3)	(65.7)	(−8.1)
NIF[a]	0	1	0	1	0
ZPE[a]	34.5	31.9	33.8	30.6	35.6
MP4SDQ/6-31G*[a]	(0.0)	(64.1)	(22.7)	(67.3)	(−9.8)
Estimated[a]	(0.0)	(61.5)	(22.0)	(63.4)	(−8.7)

[a] See footnotes to Table 1.

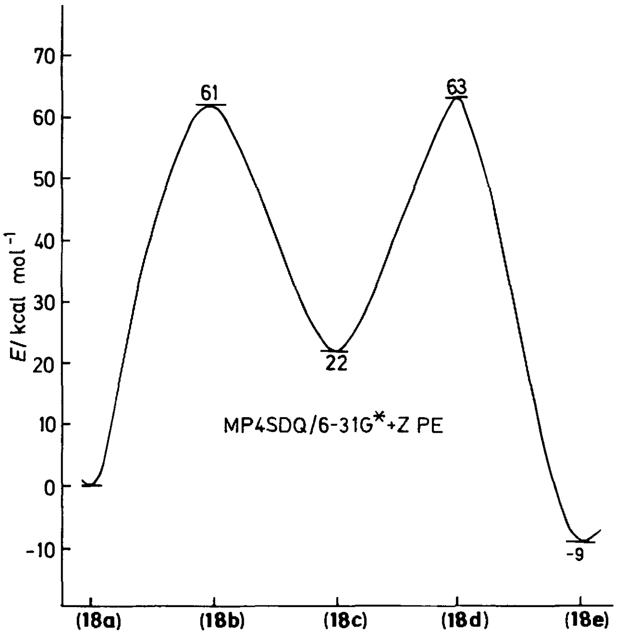


Figure 4. Schematic energy profile for the nitrile $\longrightarrow$ oxazole transformation. Energies are given in kcal mol^{-1}.

clearly indicates that the hydrogen has already been transferred in the transition state. However a considerable degree of bending is still required to form the oxazole. Thus ring closure and hydrogen transfer are quite asynchronous.

The overall reaction is slightly exothermic to the extent of −8.7 kcal mol^{-1} (Table 2). Compared with the carbene case, the isonitrile is much more stable with respect to unimolecular rearrangement in either direction. As seen in Figure 4, the isonitrile (**18c**) lies comfortably in a potential well. The energy required for it to form the oxazole is *ca.* 2 kcal mol^{-1} larger than that to convert back into the nitrile. Thus, the isonitrile is no doubt a stable intermediate during the thermal transformation being considered. As in the α-alkynone cyclisation,[5] the conversion of this direct intermediate into the cyclic product (rather than its formation) constitutes the rate-limiting step of the overall process.

It is worth noting that compared with the HCN–HNC system, the isonitrile (**18c**) is somewhat destabilised with respect to the nitrile (**18a**). As a matter of fact, the energy difference between the parent molecules HNC–HCN amounts to *ca.* 15–16 kcal mol^{-1} computed at comparable levels of theory[14] (the experimental value of HNC–HCN being 14.8 ± 2 kcal mol^{-1}).[15] However, the energy barrier required for HNC to rearrange to HCN is significantly smaller (30–31 kcal mol^{-1})[14] than that for (**18c**). This implies that, under appropriate experimental conditions, the intermediate (**18c**) could be detected spectroscopically.

In conclusion, the most significant chemical result of the present theoretical study is a proposition that the alkylidenecarbene (**17c**) can hardly be an intermediate during the cyclisation of (**17a**) whereas the isonitrile (**18c**) is quite a stable species. In addition, the rearrangement of the latter into the cyclic product (rather than its formation) constitutes the rate-determining step of the entire chemical process.

Acknowledgements

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References

1 R. F. C. Brown, F. W. Eastwood, K. J. Harrington, and G. L. McMullen, *Aust. J. Chem.*, 1974, **27**, 2393.
2 R. Bloch and P. Orvane, *Tetrahedron Lett.*, 1981, **22**, 3597.
3 T. J. Barton and B. L. Groh, *J. Org. Chem.*, 1985, **50**, 158.
4 (*a*) M. Karpf and A. S. Dreiding, *Helv. Chim. Acta*, 1979, **62**, 852; (*b*) M. Karpf, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 414; (*c*) J. C. Gilbert and B. K. Blackburn, *J. Org. Chem.*, 1986, **51**, 3656; (*d*) M. Karpf, personal communication.
5 M. T. Nguyen and A. F. Hegarty, *J. Chem. Soc., Perkin Trans. 2*, 1987, 55.
6 J. P. Ferris, R. S. Narang, T. A. Newton, and V. R. Rao, *J. Org. Chem.*, 1979, **44**, 1273, and references therein.
7 J. P. Ferris, P. C. Joshi, E. Edelson, and J. G. Lawless, *J. Mol. Evol.*, 1978, **11**, 293, and references therein.
8 B. Bigot and D. Roux, *J. Org. Chem.*, 1981, **46**, 2872.
9 J. P. Ferris and F. R. Antonucci, *J. Am. Chem. Soc.*, 1974, **96**, 2014.
10 M. R. Peterson and R. A. Poirier, Program MONSTERGAUSS, University of Toronto, 1983.

11 J. S. Binkley, J. A. Pople, and W. J. Hehre, *J. Am. Chem. Soc.*, 1980, **102**, 939.

12 R. Krishnan, M. J. Frisch, and J. A. Pople, *J. Chem. Phys.*, 1980, **72**, 4244, and references therein.

13 J. S. Binkley, R. A. Whiteside, K. Raghavachari, R. S. Seeger, D. J. Defrees, H. B. Schlegel, M. J. Frisch, and J. A. Pople, GAUSSIAN 82 program, Carnegie-Mellon University, Pittsburgh.

14 (*a*) J. A. Pople, R. Krishnan, H. B. Schlegel, and J. S. Binkley, *Int. J. Quantum Chem.*, 1978, **14**, 545; (*b*) J. A. Pople, K. Raghavachari, M. J. Frisch, J. S. Binkley, and P. v. R. Schleyer, *J. Am. Chem. Soc.*, 1983, **105**, 6389.

15 C. F. Pau and W. J. Hehre, *J. Chem. Phys.*, 1982, **86**, 321.

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