An *ab initio* and MNDO-d SCF–MO computational study of the extrusion reactions of R_2I–F iodine(III) *via* dimeric, trimeric and tetrameric transition states†

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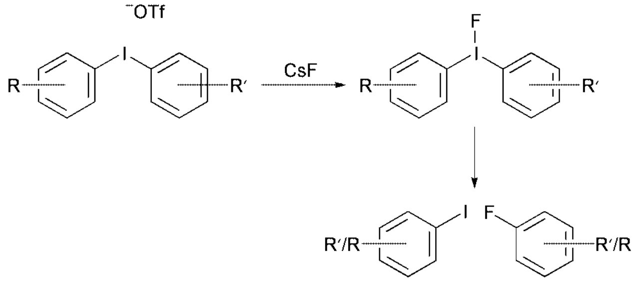
MNDO-d and *ab initio* RHF and B3LYP energies and geometries are reported for the reactant and transition states for F–R extrusion reactions of RR′I–F iodine(III) involving dimeric, and novel trimeric and tetrameric structures. The trimer is found to have unique properties deriving from novel transition state coordination between the reacting fluorine and the three iodines, which includes a significant decrease in the barrier to reaction compared to the monomer, dimer and tetramer.

Introduction

Diaryliodonium salts have received much recent attention as general reagents for the preparation of fluoroarenes (Scheme 1).[1]



Scheme 1

The ability to control and predict the regiochemical outcome of this aromatic nucleophilic substitution process is of paramount importance. We have recently reported the first comprehensive theoretical study on the mechanism of this reaction,[2] from which our key conclusion was that the regiospecificity of this reaction was controlled by transition state, and not by reactant, stability. Another new feature that we identified was the possibility of the RR′I–F reactant forming an asymmetric bridged dimer, involving a square planar iodine centre, which had not, hitherto, been considered as a factor in the mechanism of this reaction. The reactions of both the monomer and the bridged dimer were found to exhibit unusually large stereoelectronic effects at the iodine centre, derived from electron-donating and withdrawing substituents on the R groups. Here we report an extension of this study to include possible trimer and tetramer formation in the transition states of these reactions, again not, hitherto, considered to be features of this type of reaction.

Computational procedure

The geometries of all species were initially defined using the MacMolPlt[3] and CaChe programs. All putative saddle points were characterised by calculation of the force constant matrix and normal coordinate analysis. Zero point corrections were applied and found to decrease the activation enthalpies by 1.0–1.7 kcal mol^{-1}. Calculations at the RHF and B3LYP density functional level were performed using the GAUSSIAN98 program system[4] and at the semi-empirical SCF–MO MNDO-d level using the MOPAC2000 program.[5]†

Results and discussion

In our previous study, we established the basic features of the computational modelling of the extrusion reaction of R–F from RR′I–F. These included the utility of the initial location of transition states using the MNDO-d parameters in the *MOPAC2000* program, the relatively small basis set dependence of the geometries and energies, the systematic lowering of the activation enthalpies by including electron correlated methods and a justification of the use of the smaller alkynyl group, instead of a phenyl group, as a model.

Our first extension of the previous study was to use the MNDO-d procedure to evaluate the association energy per unit for the formation of cyclic oligomers $(R_2I\text{–}F)_n$. The resulting values of 10.6, 17.9 19.3 and 19.2 kcal mol^{-1} for $n = 2$–5 (Table 1) and the congruence with the other methods (RHF/3-21G(d), 9.1, 12.9, 15.1 for $n = 2$–4; B3LYP/3-21G(d), 12.2, 18.7, 20.0 for $n = 2$–4, Table 1) suggests that an extended study of the cyclic dimer (**1**), trimer (**2**) and tetramer (**5**) should reveal convergent behaviour for the predicted mechanism for this reaction.

Dimer 1 (Scheme 2)

In our previous report we showed that the *ab initio* geometries for the reactant dimer were calculated to be significantly asymmetric (I–F 2.0, 2.5–2.7 Å), whereas the MNDO-d geometry was symmetric. At the transition state, for the F–R extrusion reaction, the influence of electron-withdrawing or donating groups within R were virtually identical to the

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† Molecular coordinates, in the form of MDL Molfiles for located stationary points are integrated into this article in an enhanced on-line form as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/p2/b0/b000429o/

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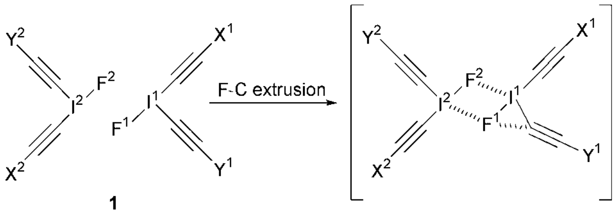
Table 1 Reactant and transition state energies (hartree), association or activation energies (kcal mol^{-1}) and imaginary normal mode wavenumber (cm^{-1}) for stationary point structures **1**–**5** at four different levels of theory

Entry	Substituents	Reactant	Association energy per unit	Transition state for F–R extrusion[a]	ν_1
1	$X^1 = X^2 = H, Y^1 = Y^2 = H$	−14276.7220	−9.1	−14276.6557 (41.6)	583 *i*
		−14284.9882	**−12.2**	**−14284.9473 (25.7)**	**418** *i*
		−14346.2180	***−7.0***	***−14346.1794 (24.2)***	***413 i***
		192.8	*−10.6*	*247.7 (54.8)*	*794 i*
2	$X^1 = X^2 = X^3 = H, Y^1 = Y^2 = Y^3 = H$	−21415.1012	−12.9	−21415.0461 (34.6)	438 *i*
		−21427.5135	**−18.7**	**−21427.4748 (24.3)**	**267** *i*
		267.3	*−17.9*	*328.3 (61.1)*	*769 i*
3[b]	$X^1 = X^2 = X^3 = CN, Y^1 = Y^2 = Y^3 = OCH_3$	−22028.5216	−13.5	−22028.4729 (30.6)	419 *i*
		223.0	*−17.6*	*277.2 (54.2)*	*726 i*
4[b]	$X^1 = X^2 = X^3 = OCH_3, Y^1 = Y^2 = Y^3 = CN$	−22028.5216	−18.7	−22028.4475 (46.5)	419 *i*
		223.0	*−20.4*	*282.6 (59.6)*	*726 i*
5	$X^1 = X^2 = X^3 = X^4 = H, Y^1 = Y^2 = Y^3 = Y^4 = H$	−28553.4824	−15.1	−28553.4211 (38.5)	476 *i*
		−28570.0263	**−20.0**	**−28569.9773 (30.7)**	**402** *i*
		350.9	*−19.3*	*413.3 (62.4)*	765 i

[a] At the levels of theory corresponding to RHF/3-21G(d), **B3LYP/3-21G(d)**, ***B3LYP/DZVP*** (hartree) and *MNDO-d* (kcal mol^{-1}). [b] Relative transition state energy **3**–**4**; +15.9, *+5.4* kcal mol^{-1}.



Scheme 2

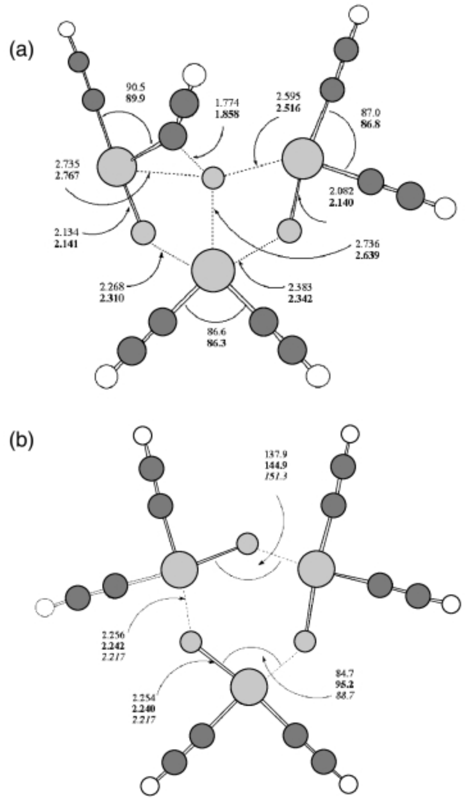


Fig. 1 Distances (Å) and angles (degrees) for (a) reactant and (b) transition state of **2** for F–C extrusion (RHF/3-21G(d), **B3LYP/3-21G(d)**, *MNDO-d*).

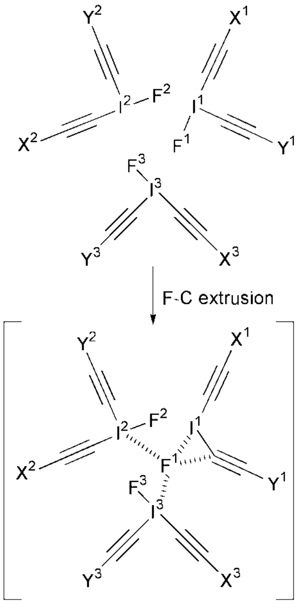
monomer values. Thus as a dimeric structure, F–R extrusion is enhanced by an electron-withdrawing group on the reacting R centre (equatorial position) and inhibited by an electron donating one.

We also investigated two other properties of the dimerisation, the entropy and derived free energy of association, and the effect solvation might have on these quantities. The gas phase enthalpy of dimer association at a standard state of 1 atmosphere (X = Y = H) is −18.2 kcal mol^{-1} (RHF/3-21G*), reduced to $\Delta G_{370} = -5.7$ kcal mol^{-1} when the enthalpy is corrected for the entropy at the typical temperature of reaction ($\Delta S_{370} = -34.6$ cal mol^{-1} K^{-1}) estimated from a rigid-rotor-harmonic-oscillator (RRHO) vibrational analysis of monomer and dimer. Application of a self-consistent-reaction-field (SCRF-PCM) solvation model, specifying acetonitrile as solvent to obtain an approximate estimate of the solvation effect, is justified by the lack of evidence of strong anisotropic hydrogen-bonding interactions with solvent from the known crystal structures of such species.[2] This correction reduces ΔH for dimer association to −15.7 kcal mol^{-1} and increases ΔS_{370} to −41.5 cal mol^{-1} K^{-1}, resulting in ΔG_{370} −0.2 kcal mol^{-1}. Further corrections for the non-electrostatic (cratic) components corresponding to translational entropy loss[6] will tend to make ΔG_{370} more positive. Given these, and other uncertainties in the calculated energies and entropies, significant concentrations of unsubstituted dimer in acetonitrile solution may not be very likely. Systems for which substituents increase the enthalpy of association (*e.g.* entry **4**, Table 1) are certainly more likely to contain oligomers.

Trimers 2–4 (Scheme 3)

The *ab initio* and MNDO-d reactant geometries for the trimer **2** were calculated to be essentially symmetric (I–F 2.254, 2.256 Å) and planar (Fig. 1).

We also studied the influence of electron-withdrawing and -donating groups on the axial and equatorial positions (Table 1, entries **3** and **4**). Different combinations of CN and OMe as representative substituents gave similar energies for the reactants, emphasizing that the trimer is symmetric and that there is equivalence in the trimer between the axial and equatorial substituents of the original monomer. In effect, the trimer provides a mechanism with no enthalpic barrier for axial–equatorial interconversion of the substituents. The presence of a significant number of low energy modes (<400 cm^{-1}) in the trimer (arising from the large iodine mass) means significant uncertainty in the use of rigid-rotor assumptions to derive the entropy, and hence the free energy, for this process. For the gas phase (X = Y = H), these estimates are ΔH −38.7 kcal mol^{-1}, ΔS −72.1 cal mol^{-1} K^{-1} and hence ΔG_{370} −12.0 kcal mol^{-1}. We were unable to obtain convergence for the SCRF solvation model, but on the basis of the very modest destabilisation calculated for the dimer (~5 kcal mol^{-1}) a negative ΔG_{370} for trimer formation is still likely. A further unfavourable contribution to the free energy of binding from the



2–4

Scheme 3

"cratic" or translational energy term should be expected, but would be compensated by increased enthalpic contributions to the binding from the appropriate electron-donating and -withdrawing substituents. Experimental studies of this aspect are clearly desirable.

For the transition state, all the *ab initio* methodologies predict an unusual feature in **2**: that the reacting F is coordinated to the three iodines simultaneously (Fig. 1). The other two fluorines remain coordinated to the neighbouring iodines. This situation leads to decreased enthalpies of activation at all the levels of theory, in comparison with the dimer **1** and tetramer **5**. The calculated activation entropy for **2** reflects this tighter structure, being -4 cal mol^{-1} K^{-1} compared with essentially zero for the dimer. The activation free energy is accordingly 1 kcal mol^{-1} higher than the enthalpy. The 3-21G(d) basis set shows a planar geometry, but with the ethynyl fragment slightly out of plane and the reacting F^1 being closer to the I^2 (2.516–2.595 Å) than to the I^1 and I^3 (2.639–2.767 Å). The remaining fluorines (F^2 and F^3) are closer to iodines I^1 and I^3, respectively, and the unique character of each unit disappears. In contrast to the *ab initio* results, the MNDO-d predicted transition state geometry does not reveal any unusual coordination for the reacting F, maintaining an open geometry for the transition state. Normal coordinate analysis of the transition stationary point revealed a single imaginary mode, an IRC analysis showing this to connect the product with a high energy conformation ($+3.0$ kcal mol^{-1}) of the trimer reactant with substantial out of plane displacement of one ethynyl fragment.

The presence of one electron-withdrawing and one electron-donating substituent can give rise to two isomeric transition states, *e.g.* **3** ($X^1 = X^2 = X^3 = CN$, $Y^1 = Y^2 = Y^3 = OMe$) and **4** ($X^1 = X^2 = X^3 = OMe$, $Y^1 = Y^2 = Y^3 = CN$). The substituents only had a significant effect at the reacting component of the trimer, since the different combinations of these substituents at the non-reacting components did not give rise to any significant changes in the energy. Again F–R extrusion is enhanced by an electron-withdrawing group on the extruding group and is inhibited by electron donation on that group. Thus the transition state of **3** was calculated to be 15.9 kcal mol^{-1} more stable than the transition state of **4**. Unlike **3**, **4** exhibits no enhanced coordination at the central fluorine, suggesting the unusual coordination in **3** might be highly sensitive to the precise nature of the groups and their substituents.

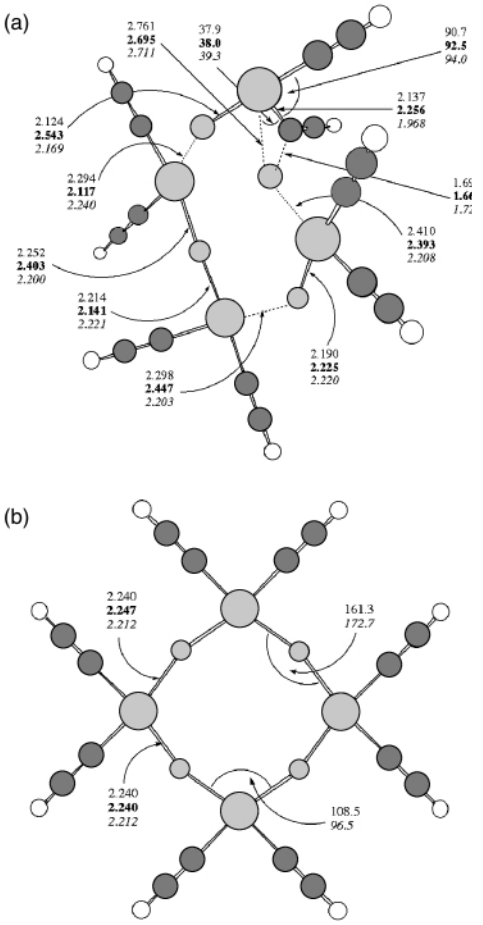


Fig. 2 Distances (Å) and angles (degrees) for (a) reactant and (b) transition state of **5** for F–C extrusion (RHF/3-21G(d), **B3LYP/3-21G(d)**, *MNDO-d*).

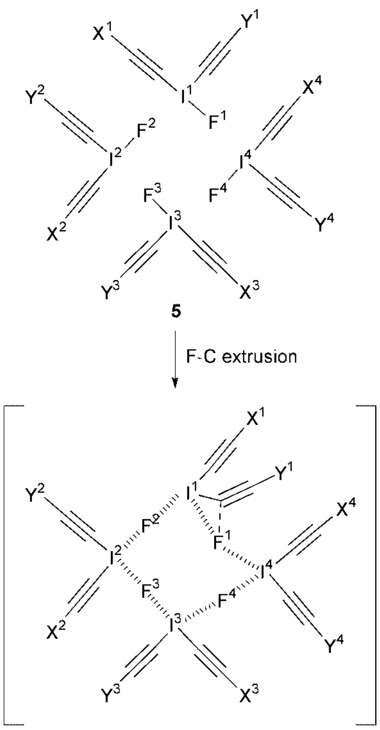
Tetramer 5 (Scheme 4)

The *ab initio* and MNDO-d methods gave different geometries for the reactant tetramer. The RHF/3-21G(d) and MNDO-d levels predict a symmetric and planar geometry. The B3LYP method leads to a boat conformation, maintaining the I–F coordination between the four components (Fig. 2). Also, the different combinations of CN and OMe gave similar reactant energies (291.7–292.5 kcal mol^{-1} at the MNDO-d level).

For the transition state, the unusually tricoordinated fluorine predicted for the trimer is again observed for the tetramer, albeit the similarity is most pronounced at the RHF/3-21G(d) level. The different methods led to similar geometries in which the reacting fluorine is coordinated to the neighbouring iodines. At the B3LYP/3-21G(d) level, the geometry seems to be the result of coordination between two dimers rather than a tetrameric coordinated structure.

Conclusions

Our computational studies of the extrusion reaction of species of the type RR′I–F have revealed several features unique to this type of reaction. We had previously noted the possibility that both the reactant and transition state could be dimeric units, although the substituent effects within these transition states appeared to be almost entirely additive compared to those of the monomers. The relatively large values for the dimerisation enthalpies suggested that higher oligomers might also be possible. The present results, based on both enthalpies and estimated entropies and derived free energies, reveal that significant concentrations of trimeric reactant may be possible, certainly in the gas phase and, quite possibly, in a polar solvent such as acetonitrile. The structure of the trimer, in contrast to



Scheme 4

the dimer, may be entirely symmetrical. The trimer may also present a purely entropically controlled pathway for axial–equatorial interconversion of the R and R′ groups. We believe, on this basis, therefore, that the monomer-based pseudorotation mechanism proposed by Grushin[7] may have a competitive alternate pathway. We are in the process of establishing whether the crystal structure of the species Ph_2I–F does indeed correspond to a cyclic dimer, trimer, tetramer or other oligomer. The transition state for disproportionation to R–I and R–F deriving from the trimer does display unusual coordination around the reacting F, which suggests extra stabilisation *via* this mode. Hence we conclude by proposing this transition state as a possible reactive entity in this particular reaction. If such aggregations are possible, then the possibility of participation of other counter ions in these cyclic structures arises. This would be particularly true for the conditions employed to achieve ^{18}F fluoridation for use in positron emission studies,[2] where $^{18}F^-$ ions are used only in trace quantities in the presence of other counter ions, such as tosylate. We will report on this aspect in a future article.

Acknowledgements

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