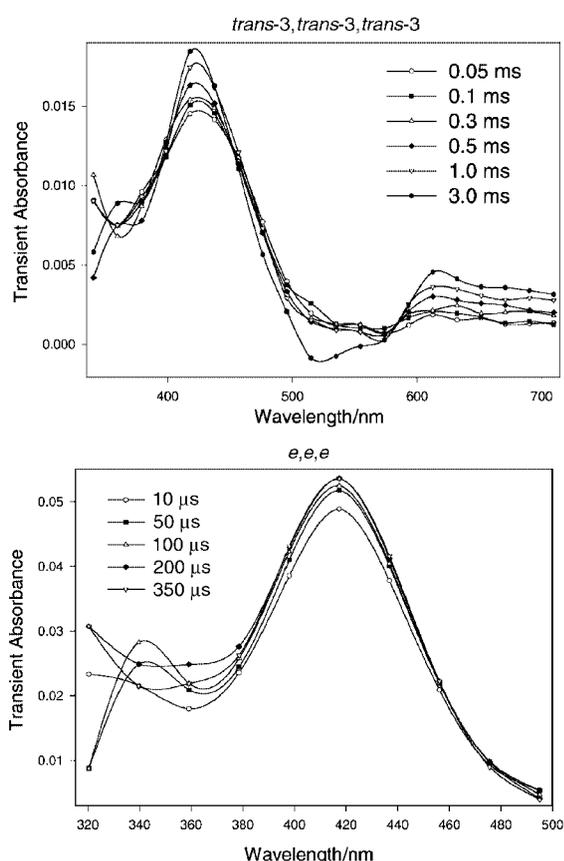




**Table 1** Site of OH addition, standard heat of formation (AM1, kJ mol<sup>-1</sup>) relative to most stable isomer and  $F_r$ , the free valence index, for the nine symmetry distinct isomers of the *trans*-3,*trans*-3,*trans*-3 anions and the 18 isomeric *e,e,e* anions, C<sub>60</sub>[C(COOH)<sub>2</sub>]<sub>3</sub>OH<sup>-</sup>

Addition to <i>e,e,e</i> isomer			Addition to <i>trans</i> -3, <i>trans</i> -3, <i>trans</i> -3 isomer		
Position	Energy (AM1)/kJ mol <sup>-1</sup>	$F_r$ index	Position	Energy (AM1)/kJ mol <sup>-1</sup>	$F_r$ index
10	17.8	0.1536	21	17.9	0.1490
13	14.4	0.1461	8	28.6	0.1400
7	33.4	0.1192	24	16.5	0.1736
8	26.2	0.1295	25	18.5	0.1676
28	17.7	0.1703	23	17.4	0.1640
26	20.1	0.1734	43	12.9	0.1710
30	10.7	0.1787	42	15.7	0.1585
24	5.1	0.1768	41	5.9	0.1780
29	17.7	0.1707	22	0.0	0.1785
25	25.3	0.1369			
27	5.6	0.1788			
45	5.8	0.1790			
47	7.5	0.1790			
12	0.0	0.1739			
46	11.1	0.1757			
6	9.2	0.1721			
9	12.1	0.1693			
11	14.2	0.1626			



**Fig. 2** Transient electronic spectra obtained on reaction of hydroxyl radical with the water-soluble malonic acid fullerene derivatives, *trans*-3,*trans*-3,*trans*-3 and *e,e,e*, showing unimolecular growth in absorption on the ms timescale.

energies for series of molecules.<sup>9</sup> Instead, in order to determine the most thermodynamically stable site of the HO<sup>•</sup> attack, calculations using the semi-empirical AM1 method<sup>10</sup> have been carried out on the closed-shell product of the reaction of hydroxyl radical and the radical anion C<sub>60</sub>[C(COOH)<sub>2</sub>]<sub>3</sub><sup>-•</sup>. The HO<sup>•</sup> radical was added to each of the symmetry-distinct vertices of the *trans*-3,*trans*-3,*trans*-3 and *e,e,e* cage isomers of the anion, leading to the closed-shell species, C<sub>60</sub>[C(COOH)<sub>2</sub>]<sub>3</sub>OH<sup>-</sup>, the structure of which was then fully geometrically optimised to obtain its energy (Table 1). This approach of course assumes that the relative thermodynamic stabilities of

these closed-shell hydroxide anions parallels the stabilities of the structurally corresponding hydroxyfullerene radicals. Test calculations indicate that this is a reasonable assumption: calculated UHF energies for the radicals, though expected *a priori* to be less reliable, were found to show a general correlation with those of the corresponding closed-shell anion. In order to interpret the more reliable anion energies, we have also carried out calculations of free valence indices using Hückel molecular orbital theory.

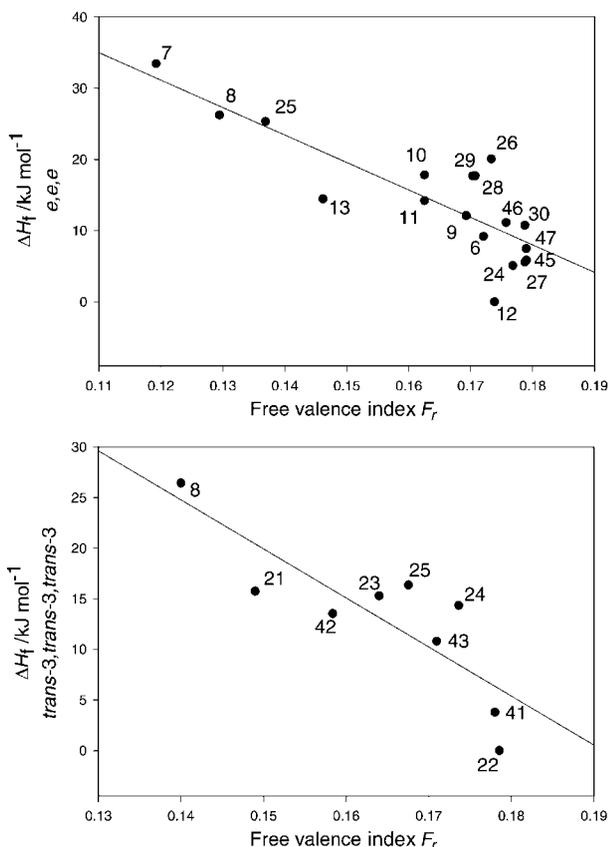
The free valence index  $F_r$ , defined by Coulson<sup>11</sup> [eqn. (1)],

$$F_r = N_{\max} - N_r \quad (1)$$

measures the ease of attack of free radicals at an atom  $r$  in a conjugated  $\pi$  system where  $N_r$  is the sum of  $\pi$  bond orders over all bonds joining atom  $r$  to the remainder of the  $\pi$  system.  $N_{\max}$  is the maximum value of this sum and depends on how many other  $sp^2$  carbons are attached to the atom in question:  $N_{\max}$  is  $\sqrt{3}$  for an  $sp^2$  carbon attached to  $m$  others. This index has been successfully applied<sup>12</sup> in the creation of a simple model for radical addition to fullerenes. In particular, it was shown that the *final product* arising from radical addition could be predicted by assuming *initial attack* at the position of highest free valence. In the present work, these free valence indices are calculated on bare C<sub>60</sub> cages where a double bond and its four neighbours have been removed from the  $\pi$  system for each site occupied by a malonic acid addend. Separate calculations are made for the two isomers *trans*-3,*trans*-3,*trans*-3 and *e,e,e*.

Fig. 3 displays the correlations for each isomer between the value of the free valence index and the heat of formation of the corresponding C<sub>60</sub>[C(COOH)<sub>2</sub>]<sub>3</sub>OH<sup>-</sup> anion, depending on the position of the HO<sup>•</sup> group. The correlation is reasonable ( $r^2 = 0.70$ ) and both methods give a similar set of preferred sites for the attack of hydroxyl radical, since high values for the free valence indices correlate with low heats of formation of the product. The range of heats of formation (AM1) of these isomeric anions is 25 kJ mol<sup>-1</sup> for the malonic acid derivative *trans*-3,*trans*-3,*trans*-3 and 35 kJ mol<sup>-1</sup> for the *e,e,e* derivative. Calculated heats of formation using the PM3 Hamiltonian correlate well with the AM1 results ( $r^2 = 0.869$  (*e,e,e*), 0.936 (*trans*-3,*trans*-3,*trans*-3)), and lead to the same set of preferred sites for final attachment.

The following conclusion may be drawn from this correlation: the ease of attack of the hydroxyl radical on a particular position is reflected in a greater calculated stability for the corresponding hydroxide anion. For a highly reactive radical such as HO<sup>•</sup>, it is likely that the final energy of the product will



**Fig. 3** Correlation between the free valence indices and the heats of formation (AM1) of the isomeric anions *e,e,e* and *trans-3,trans-3,trans-3*  $C_{60}[C(COOH)_2]_3OH^-$ . The labels correspond to the position of the hydroxy group on the  $C_{60}$  cage (see Fig. 1).

correlate with the reactivity of the site of attachment. For *closed-shell* fullerene derivatives,<sup>13–15</sup> calculated thermodynamic stabilities have already been shown to parallel the predictions of a model which uses free valence.<sup>12</sup> The correlation of  $F_r$  and anion stability found here supports the anion calculations as good predictors of the relative stabilities of the actual radical products. Thus whether the positional rearrangement of the hydroxy group around the cage, from the initial site of attack at random to the most stable one, is under kinetic or thermodynamic control, our calculations should give an indication of its final position. Taking a typical Arrhenius  $A$  factor for a unimolecular process to be between  $1 \times 10^{11} \text{ s}^{-1}$  and  $1 \times 10^{15} \text{ s}^{-1}$ , a half-life of 0.1 ms at 300 K suggests an activation energy in the range 40–60  $\text{kJ mol}^{-1}$ . The fact that this is higher than the energy range of all the hydroxyfullerene anions does not of course prevent a rearrangement process to the thermodynamically most stable isomer; it is only required that, if activation control is in place, then the activation energies should parallel the product stabilities as suggested by the observed  $F_r$ –stability correlation.

Clearly, with such a small range of energies, the final radical product for this stage of the reaction may be a mixture of several of the more stable isomers. The pattern of stability of these species is that the most reactive positions towards an attacking radical (and the most stable final products) are the ones in which a hydroxy group has added to a carbon atom that is contiguous to a malonic acid group (sites number 3 and 21 for *e,e,e*; 22 and 41 for *trans-3,trans-3,trans-3*), or, in the case of *e,e,e* isomer, the sites corresponding to a further equatorial addition of malonate (27 and 45). The former are reminiscent of the reaction of carbon centred radicals, where contiguous addition leads to allylic and cyclopentadienyl radical type structures. It has been stated<sup>16</sup> that the reason for this is not

steric protection of the unpaired electron, but increased C–C hyperconjugation due to the steric relationship of the half-filled  $p$ -orbital and the C–C  $\sigma$  bond on the next atom. Hyperconjugation cannot account for the relative stabilities of these hydroxyfullerene anions; but hydrogen bonding between the carboxylic acid groups and the added hydroxy group would be a stabilising factor. In a model based on free valence, the rôle of the coordination number in the definition implies that contiguous addition will tend to be favoured as long as the average  $\pi$ -bond order exceeds  $\sqrt{3} - \sqrt{2} \approx 0.32$ . For the *e,e,e* isomer, the two further addition sites which are favoured (27, 45) are related to the formation of the equatorial tetra-adduct  $C_{60}[C(COOH)_2]_4$ , which has the fourth malonic acid group across the double bond defined by them.<sup>17</sup> In fact, if an average free valence index is taken for each formal double bond, all the abundant isomers on the pathway for sequential addition of malonate groups are predicted. This is consistent with the fact that electronic considerations have been found<sup>17</sup> to predict the sequence of attack in a similar series of adducts, in a model using AM1 LUMO coefficients. The finding that free valence indices parallel more sophisticated calculations in this case is a further illustration of the continuing utility of simple graph-theory based methods in the rationalisation of experimental data. In this case our results suggest that after attack of the hydroxyl radical at the first encountered double bond, migration subsequently takes place to the position of highest free valence.

## Acknowledgements

The authors acknowledge the EU TMR Scheme (Network Contract FMRX-CT98-0192 ‘BIOFULLERENES’) for financial support of this research. The transient electronic spectra and kinetics of some of the mono-hydroxylated fullerene radicals were obtained by pulse radiolysis at the Paterson Institute for Cancer Research Free Radical Research Facility, Manchester, UK with the support of the European Commission through the Access to Large-Scale Facilities activity of the TMR Programme.

## References

- 1 P. J. Krusic, E. Wasserman, P. N. Keizer, J. R. Morton and K. F. Preston, *Science*, 1991, **254**, 1183.
- 2 M. Walbinder and H. Fischer, *J. Phys. Chem.*, 1993, **97**, 4880.
- 3 J. R. Morton, F. Negri and K. F. Preston, *Acc. Chem. Res.*, 1998, **31**, 63.
- 4 N. M. Dimirtijevic, *Chem. Phys. Letters*, 1992, **194**, 457.
- 5 N. M. Dimirtijevic, P. V. Kamat and R. W. Fessenden, *J. Phys. Chem.*, 1993, **97**, 615.
- 6 R. V. Bensasson, M. Brettreich, J. Frederiksen, H. Göttinger, A. Hirsch, E. J. Land, S. Leach, D. J. McGarvey and H. Schönberger, *Free Radical Biol. Med.*, 2000, **29**, 26.
- 7 G. V. Buxton, C. V. Greenstock, W. P. Helman and A. B. Ross, *J. Phys. Chem. Ref. Data*, 1998, **17**, 513.
- 8 P. R. Birkett, P. B. Hitchcock, H. W. Kroto, R. Taylor and D. R. M. Walton, *Nature*, 1992, **357**, 479; F. Diederich, L. Isaacs and D. Philp, *Chem. Soc. Rev.*, 1994, **23**, 243.
- 9 T. Clark, *A Handbook of Computational Chemistry*, John Wiley and Sons, New York, 1985, ch. 3.
- 10 M. J. S. Dewar, E. G. Zoebisch, E. F. Healy and J. J. P. Stewart, *J. Am. Chem. Soc.*, 1985, **107**, 3902.
- 11 C. A. Coulson, *Faraday Discuss. Chem. Soc.*, 1947, **2**, 9.
- 12 K. M. Rogers and P. W. Fowler, *Chem. Commun.*, 1999, 2357.
- 13 S. J. Austin, P. W. Fowler, J. P. B. Sandall, P. R. Birkett, A. G. Avent, A. D. Darwish, H. W. Kroto, R. Taylor and D. R. M. Walton, *J. Chem. Soc., Perkin Trans. 2*, 1995, 1027.
- 14 P. A. Cahill and C. M. Rohlfing, *Tetrahedron*, 1996, **52**, 5247.
- 15 B. W. Clare and D. L. Kepert, *J. Mol. Struct. (THEOCHEM)*, 1995, **340**, 125; B. W. Clare and D. L. Kepert, *J. Mol. Struct. (THEOCHEM)*, 1995, **358**, 79.
- 16 R. Taylor, *Lecture Notes on Fullerene Chemistry: A Handbook for Chemists*, Imperial College Press, London, 1999, p. 105.
- 17 A. Hirsch, I. Lamparth and T. Grösser, *J. Am. Chem. Soc.*, 1994, **116**, 9385.