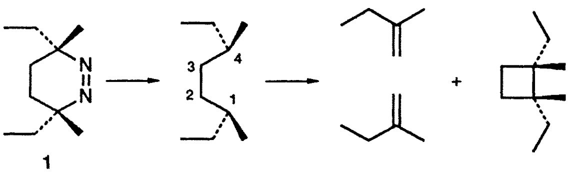
Deazetation of a Bicyclic Azo Compound: Product and Mechanistic Studies

Christopher J. Samuel
Department of Chemistry, University of Warwick, Coventry, UK, CV4 7AL

In the deazetation of 7,8-diazabicyclo[4.2.2]dec-7-ene **2**, the product distributions from direct and sensitised photolyses are different, as would be expected if a spin correlation effect operates. A larger difference, however, is found between the distributions from the two nominally singlet processes, thermolysis and the direct photolysis. Several trivial explanations for this are ruled out, and two explanations are put forward, involving the intermediacy of either a diazenyl biradical or two singlet electronic states of the tetramethylene biradical, cyclooctanediyl.

For many years, cyclic azo compounds have been used as models to mimic the behaviour of biradicals.[1] One of the earliest studies of this type was that of Bartlett and Porter[2] who modelled the behaviour of 1,4-biradicals in [2 + 2] cycloaddition reactions[3] by considering the behaviour of the monocyclic azo compound **1** which loses nitrogen and gives hydrocarbon products as shown in Scheme 1. It was clear from this study that the triplet sensitised process gave a very different product distribution from the other two processes, both nominally singlet.



1

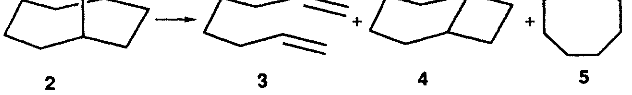
Method	Cleavage/coupling	*cis/trans*
Δ(150 °C)	1.1	17.2
hν (direct)	1.6	10.0
hν (sens)	3.9	1.4

Scheme 1

They explained this by noting that, for a triplet biradical to form products in their singlet ground states, spin inversion is necessary, so such processes are likely to be slower than those of the corresponding singlet biradicals, leading to longer lifetimes for triplet biradicals. Thus, for the triplets, spin conservative processes, such as rotation about single bonds, can compete more effectively with formation of stable products. Rotation about C^1–C^2 or C^3–C^4 followed by inter-system crossing (isc) and ring closure leads to cyclobutane with loss of stereochemical memory. Rotation about C^2–C^3 leads from an initial *syn* or *gauche* conformation, which can either couple or cleave, to a (presumably more stable) *trans* conformer, which can only cleave, and results in the observed enhanced cleavage from the triplet. The phenomenon, which arises largely from an extended lifetime for the triplet biradical, because of the spin forbiddenness, is known as a spin correlation effect (sce), and, since the original report, has been widely observed.[1]

The explanation, however, was challenged by Stephenson and Brauman,[4] soon after the original postulate. They suggested, instead, that photochemically-produced triplet biradicals were formed with substantial excess vibrational energy, and thus behaved differently from the thermally produced singlet biradicals. More recent work, however, has shown that some of the assumptions on which they based their criticisms are not valid, and the explanation in terms of an sce has come to be generally accepted.[1] It accounts for most, though not all[5] of the differences between the behaviour of singlet and triplet biradicals.

We have recently reported[6] a detailed study of the stereochemistry of deazetation of 7,8-diazabicyclo[4.2.2]dec-7-ene **2**, and presented the product distributions without comment (Scheme 2). This case was typical in that the sensitised and direct photolyses differed, both in stereochemistry and in product proportions, as would be expected if an sce operates. There was, however, an even larger difference between the two nominally singlet processes, thermolysis and direct photolysis, and it is on this phenomenon which this report concentrates.

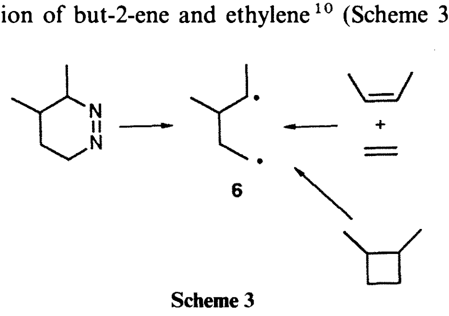


Method	**3**	**4**	**5**
Δ(170 °C)	47	35	18
hν (direct)	78	17	5
hν (sens)	74	20	6

Scheme 2

This latter difference was smaller, though still apparent, in the classic work of Bartlett and Porter[2] (Scheme 1), but has received little comment. Since that early report, this type of behaviour has been observed for a number of other azo compounds,[1] and also, though less often, for diazo compounds.[7] It has received less comment, possibly because most of the cases in the literature are subject to trivial explanations, of which some examples are given in the discussion.

It is appropriate to recognise, at this stage, that the basic assumption underlying the use of azo compounds as model systems is that nitrogen is lost to give a biradical without any major change in the carbon skeleton. An example where it seems sound is in the studies by Dervan which show good agreement between the behaviour of biradical **6** when generated from the azo compound,[8] by pyrolysis of the cyclobutane,[9] and in the cycloaddition of but-2-ene and ethylene[10] (Scheme 3). However, increasing numbers of exceptions have been uncovered, in which the departing nitrogen molecule exerts a major influence on the observed chemistry.[11]



Scheme 3

Table 1 Product ratios from deazetation of diazabicyclodecene **2**

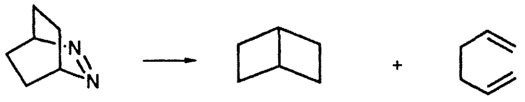
Conditions	Ratio 3:4	5:4
Δ, 180 °C	1.388	0.500
170	1.359	0.504
160	1.337	0.505
150	1.321	0.507
140	1.309	0.509
130	1.265	0.513
Δ, 30 °C[a]	0.981 ± 0.064	0.551 ± 0.042
hν, direct	4.751 ± 0.030	0.300 ± 0.003
hν, sensitised	3.696 ± 0.095	0.285 ± 0.006

[a] Extrapolated from higher temperatures.

Results

We report here further studies of the deazetation of 7,8-diazabicyclo[4.2.2]dec-7-ene **2**, aimed at elucidating the intriguing difference between the thermal and direct photochemical processes.[6] We have carried out a number of control experiments and measured the product ratios more carefully, over a range of carefully controlled conditions, to afford the results given in Table 1. In discussing these, we consider first some of the trivial explanations for the phenomenon, which we are able to rule out, and then move on to some rather more fundamental considerations.

Thermally Labile Photoproducts.—In many cases the high energy biradical is able to form a thermodynamically unstable product, which is kinetically stable at the photolysis temperature, but which is thermally labile at the temperature needed for the thermolysis. For the example given in Scheme 4,[12] published activation parameters[13] show that, at 220 °C, bicyclo[2.2.2]hexane reacts about a hundred times faster than it is formed, so its absence from the products of thermolysis is hardly surprising, and gives no indication of the behaviour of the biradical. Many thermally labile compounds have been synthesised from azo compounds photochemically, by taking advantage of this.[14]



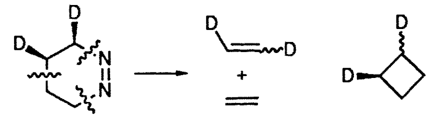
Method		
Δ(220 °C)	0	100
hν (direct)	42	58
hν (sens)	33	67

Scheme 4

In the present case, octadiene and cyclo-octene are known[15] to interconvert at 720 °C in a flow system. Under these conditions, vinylcyclohexane is also formed, and would thus be diagnostic of secondary thermolysis, but is absent from the reaction of the azo compound. *cis*-Bicyclo[4.2.0]octane undergoes a retro-[2 + 2] cycloaddition at 450 °C,[16] to give cyclohexene which is also absent from the thermal deazetation of **2**. All three of the observed products are stable at temperatures well above those involved in this work,[6] and even *trans*-bicyclo[4.2.0]octane, which is known not to be formed, is stable for 24 h at 250 °C. Furthermore, a control experiment was carried out in the stereochemical study,[6] in which **2** was deazetised in the presence of [1,8-$^2H_2$]-**3**, by each of the three processes. In each case, the ^{2}H NMR spectrum of the products showed that the deuterium was present only in the octadiene, demonstrating that there is no thermal (or photochemical) reaction of **3**.

Vibrationally Hot Biradicals.—We considered that the singlet biradicals from thermolysis and direct photolysis might have been formed with different internal vibrational energies, and thus reacted differently (see the alternative to the sce, proposed by Stephenson and Brauman,[4] and discussed above). However, even a short-lived singlet biradical containing 22 atoms should undergo collisional deactivation in solution very rapidly. A typical recent example of 'chemical activation'[17] concerns the deazetation of an azo compound to form bicyclobutane, with only 10 atoms, which does show the effect of excess vibrational energy on the product distribution, but only in the gas phase. The dimethyl analogue (18 atoms) shows no such effect in the gas phase, and neither shows any such effect in solution.

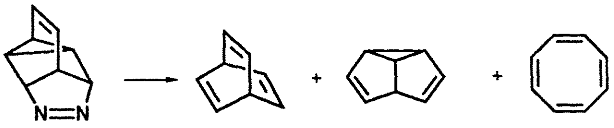
Concerted Retro-[2 + 2 + 2] *Cycloreversion.*—The thermal reaction may include a component of the symmetry allowed, concerted, σ2s + σ2s + σ2s cleavage of C–N, C–C and C–N bonds, in competition with the biradical process (*cf.* Scheme 5), leading to extra cleavage product in the thermal reaction. Berson[18] has suggested criteria which rule out such a process unless the C–C bond to be broken is severely strained, but Dervan[8,19] has provided stereochemical evidence which shows a substantial concerted component even for unstrained C–C bonds.



81% retention 56%

Scheme 5

The concerted process may account for the spectacular case of Zimmerman[20] (Scheme 6) where the low decomposition temperature of the azo compound **7** (< 80 °C) implies that anchimeric assistance by the C–C bond facilitates the loss of nitrogen, though he has argued cogently that this does not invalidate his conclusions about the di-π-methane rearrangement.



7

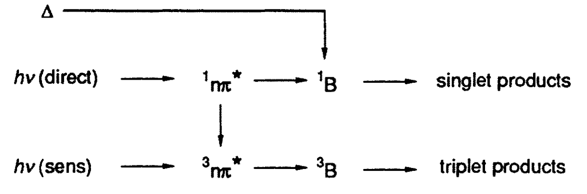
Method			
Δ(80 °C)	100	0	0
hν (direct)	24	73	3
hν (sens)	0	100	0

Scheme 6

In the present case, there is no kinetic evidence for concertedness, since the decomposition temperature is normal; at the lowest temperature in Table 1, 130 °C, the reaction time of 68 h represents only 10% conversion. Furthermore, even a substantial concerted component leading to cleavage would not affect the conclusions since if some of the diene came by this route the difference between the singlet biradicals generated by the thermal and direct photochemical processes would be even greater.

Temperature Dependence.—It is obvious that the thermal and direct photochemical reactions occur at different temperatures and, if the same biradical is formed in both cases, but has different activation energies for the various processes leading from it, then the temperature dependence, alone, might account for the difference. We have studied the thermolysis at various temperatures (130–180 °C), and find a very small temperature dependence, which is interesting in its own right, and about which we comment below. Extrapolating the data to the photolysis temperature (*ca.* 30 °C) actually increases the critical differences, as Table 1 shows.

Inter-system Crossing.—Inter-system crossing from $^1n\pi^*$ azo compounds is generally a fairly slow process,[1,21] though, in a few cases, it is believed to compete with loss of nitrogen.[22] In the present case, Scheme 7 would imply that the 'singlet product distribution' is given by the thermolysis data extrapolated to the photolysis temperature, as above. Further, the 'triplet product distribution' would be given by the sensitised photolysis. The direct photolysis would then be a combination of the two, and should thus lie between them, which it clearly does not.



Scheme 7

More generally, if there are only two independent pathways from azo compound to products *e.g. via* one singlet and one triplet biradical, as implied by this scheme, then the three observed product distributions must each be linear combinations of the two independent product distributions defined as above, and are thus linearly dependent in the terms of linear algebra. If this were so, the determinant formed from the ratios in Table 1 would be zero.

$$\text{Det} = \begin{vmatrix} 0.981 \pm 0.064 & 1 & 0.551 \pm 0.042 \\ 4.751 \pm 0.030 & 1 & 0.300 \pm 0.003 \\ 3.696 \pm 0.095 & 1 & 0.285 \pm 0.006 \end{vmatrix} = 0.321 \pm 0.056$$

In fact, the determinant differs from zero by more than five standard deviations, *i.e.* there are at least three linearly independent product distributions and thus at least three independent pathways from the azo compound to the final products.

Discussion

The considerations above show that we have an azo compound from which the thermal and direct photochemical pathways do, indeed, give substantially different product distributions. Furthermore we have been able to rule out a number of trivial explanations for this. We thus have a phenomenon of some basic significance. We put forward two further possible explanations, which seem to be more fundamental.

One Bond or Two Bond Cleavage.—This has long been a contentious issue, and we have summarised the evidence for one bond cleavage elsewhere.[23] A possible explanation for the present results is that one bond cleavage leads to an alkyl diazenyl biradical, which could be involved in either of two ways. Firstly, both the thermal and photochemical pathways involve stepwise cleavage, in which case the problem remains the same. Instead of needing to explain why two superficially identical carbon–carbon biradicals give different products, it is necessary to explain why two superficially identical alkyl diazenyl biradicals give different products. In order to do this it would be necessary to postulate two electronic states of the diazenyl radical being formed from the ground and excited singlet states of the azo compound. This is the way in which Adam accounted for the stereochemical results on deazetation of diazabicycloheptene.[24]

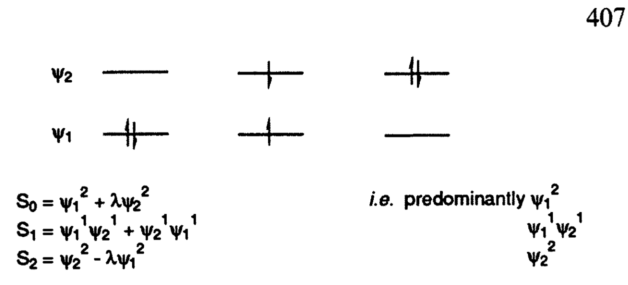


Fig. 1 Singlet electronic states of a biradical

Alternatively, of the two pathways, one involves one bond and the other involves two bond cleavage. The diazenyl biradical lives long enough, before losing nitrogen, to form the carbon–carbon biradical in a conformation different from that formed by the direct two bond cleavage mechanism. We recently suggested[23] conformational change of this sort in a diazenyl biradical in order to account for the surprising stereochemistry of the photochemical deazetation of diazabicyclo-octene.

While this could give an explanation for the present results in general terms, the conformational flexibility of the eight membered ring in cyclo-octanediyl is so much greater than that of the cyclopentanediyl discussed by Adam[24] and the cyclohexanediyl studied by us,[23] that a detailed analysis would be unduly speculative. In fact, the stereochemical results fit very well with conformational changes in a carbon–carbon biradical after two bond cleavage. Ideally, this question could be investigated by a study of leaving groups other than nitrogen and comparison of product distributions as 'fingerprints'. A number of potential precursors to cyclo-octanediyl was synthesised, but none would eliminate at a low enough temperature to compare with the results for the azo compound.

Electronic States of the Biradical.—An attractive alternative which can lead to verifiable predictions is based on an analysis of the electron states of the biradical, which we have recently reported.[25] In summary, even within the singlet manifold, there are three biradical states (Fig. 1),[26] and, in the thermolysis, the closed shell ground state should correlate with the closed shell biradical state (S_0), whereas, in the direct photolysis, the open shell $^1n\pi^*$ excited state should correlate with the open shell biradical state (S_1). Even if some leakage between states were to occur (a probable event near an orbital degeneracy) there might still be a significant difference between the thermal and photochemical reactions. The possible involvement of two singlet electronic states of a biradical has been postulated by Zimmerman in connection with the di-π-methane rearrangements.[20]

Detailed consideration of through bond (TB) and through space (TS) interactions between the half-filled orbitals in the biradical[27] led to two predictions about the difference to be expected. Firstly, regardless of the relative importance of TB and TS, the photochemical deazetation of an azo compound should be less stereospecific than the thermal reaction. This was in fact what was observed in the case of azo compound **2**[6] and also by Bartlett and Porter.[2] Secondly, depending on the relative ordering of TB and TS, the cleavage:coupling ratio should be higher or lower for the thermolysis. The experimental results fit better with TS being the dominant mode of interaction, and this may be a consequence of a geometry of the diyl which favours TS rather than TB. Some of the implications of this analysis have been discussed by Zimmerman,[28] but only for the case in which TB dominates.

Temperature Dependence.—We noted above that the product distribution in the thermal reaction shows very little dependence on temperature, corresponding to partitioning of the biradical with $\Delta\Delta H^{\ddagger} < 3$ kJ mol^{-1} for the 3:4 ratio. This implies either that all the activation energies are accidentally very close to one another, or that they are all close to zero, a more reasonable conclusion and one that is consistent with calculations on the parent tetramethylene biradical.[29] Baldwin has recently studied the parent tetramethylene, comparing static and shock tube pyrolyses to cover a temperature range of over 400 K and found very little variation in the product distribution.[30]

Conclusions

We have shown that there is a real difference between the behaviour of an azo compound on thermal and direct photochemical deazetation, and that it is not owing to any of a number of trivial explanations. We have been unable to distinguish between two significant alternative explanations. While there is a growing tendency to discuss the deazetation in terms of one-bond cleavage to give diazenyl biradicals we point out here that two different electronic states of the biradical can equally well account for the difference.

Experimental

The synthesis of 7,8-diazabicyclo[4.2.2.]dec-7-ene **2** and studies of the structure and stability of the products of its deazetation and of *trans*-bicyclo[4.2.0]octane have been reported previously.[6]

The data in Table 1 for the thermal reaction were obtained by sealing a solution of diazabicyclodecene (1%) in cyclohexane (0.1 cm^3) under nitrogen in a pyrex tube. For each run, four tubes were heated at each temperature in the oven of a Pye Unicam 204 gas chromatograph for the length of time necessary to cause *ca.* 10% reaction. The tubes, still sealed, were cooled in water. For the direct photolysis, similar tubes were strapped to the water cooling jacket of a 500 W medium pressure mercury lamp and irradiated for a sufficient length of time to produce about 10% conversion. For the sensitised photolysis, a solution of the azo compound (1%) and 3-methoxyacetophenone (0.4%) in cyclohexane (0.3 cm^3) was placed in each of four 1 mm quartz UV cells, sealed with a serum cap, deoxygenated by bubbling nitrogen, irradiated in Rayonet type photochemical reactor fitted with '300 nm' lamps to about 2% conversion, and transferred to a sealable vial. All samples were stored in liquid nitrogen until analysis and analysed on a single day.

Analysis was by GC using a 15 m × 0.3 mm OV1 fused silica capillary column in a Carlo Erba 4250TP instrument fitted with a Grob type split/splitless injector, with electronic integration using a Pye Unicam DP88 computing integrator. Each tube was analysed to give at least three concordant analyses. To minimise any possible effects of instrumental drift, the samples were analysed in a semi-random order in that the first tube of each temperature or photolysis type was analysed before any second tube *etc.*

The whole sequence was repeated, both sets of data for thermolysis were fitted to the Arrhenius equation for the extrapolation, and then averaged to give the extrapolated result in Table 1. The two sets of data for direct and sensitised photolysis were similarly averaged.

References

1 P. S. Engel, *Chem. Rev.*, 1980, **80**, 99.
2 P. D. Bartlett and N. A. Porter, *J. Am. Chem. Soc.*, 1968, **90**, 5317.
3 P. D. Bartlett, *Quart. Rev. Chem. Soc.*, 1970, **24**, 473.
4 L. M. Stephenson and J. I. Brauman, *J. Am. Chem. Soc.*, 1971, **93**, 1988; L. M. Stephenson and T. A. Gibson, *J. Am. Chem. Soc.*, 1974, **96**, 5624.
5 *e.g.* C. Doubleday, J. W. McIver and M. Page, *J. Am. Chem. Soc.*, 1982, **104**, 6533.
6 C. J. Samuel, *J. Chem. Soc., Perkin Trans. 1*, 1989, 1259.
7 H. E. Zimmerman and C. J. Samuel, *J. Am. Chem. Soc.*, 1975, **97**, 4025.
8 P. B. Dervan, T. Uyehara and D. S. Santilli, *J. Am. Chem. Soc.*, 1979, **101**, 2069; P. B. Dervan and T. Uyehara, *J. Am. Chem. Soc.*, 1979, **101**, 2076.
9 H. R. Gerberich and W. D. Walters, *J. Am. Chem. Soc.*, 1961, **83**, 3935; 4884.
10 G. Scacchi, C. Richard and M. H. Back, *Int. J. Chem. Kinet.*, 1977, **9**, 513; G. Scacchi and M. H. Back, *Int. J. Chem. Kinet.*, 1977, **9**, 525.
11 *e.g.* D. E. Reedich and R. S. Sheridan, *J. Am. Chem. Soc.*, 1988, **110**, 3697; 1985, **107**, 3360; R. S. Sheridan, *J. Am. Chem. Soc.*, 1983, **105**, 5140; R. Askani, T. Hornykiewytsch and K. M. Muller, *Tetrahedron Lett.*, 1983, **24**, 5513.
12 S. G. Cohen and R. Zand, *J. Am. Chem. Soc.*, 1962, **84**, 586; W. D. K. Clark and C. Steel, *J. Am. Chem. Soc.*, 1971, **93**, 6347.
13 P. S. Engel, R. A. Hayes, L. Kiefer, S. Szilagyi and J. W. Timberlake, *J. Am. Chem. Soc.*, 1978, **100**, 1876; M. J. Goldstein and M. S. Benzon, *J. Am. Chem. Soc.*, 1972, **94**, 5119.
14 W. Adam and O. De Lucchi, *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 762; H. Meier and K.-P. Zeller, *Angew. Chem., Int. Ed. Engl.*, 1977, **16**, 835.
15 J. K. Crandall and R. J. Watkins, *J. Org. Chem.*, 1971, **36**, 913.
16 J. E. Baldwin and P. W. Ford, *J. Am. Chem. Soc.*, 1969, **91**, 7192.
17 M. H. Chang, R. Jain and D. A. Dougherty, *J. Am. Chem. Soc.*, 1984, **106**, 4211.
18 J. A. Berson, S. S. Olin, E. W. Petrillo and P. Bickart, *Tetrahedron*, 1974, **30**, 1639.
19 P. B. Dervan and D. S. Santilli, *J. Am. Chem. Soc.*, 1980, **102**, 3863.
20 H. E. Zimmerman, R. J. Boettcher, N. E. Buehler, G. E. Keck and M. G. Steinmetz, *J. Am. Chem. Soc.*, 1976, **98**, 7680.
21 P. S. Engel, D. E. Keys and A. Kitamura, *J. Am. Chem. Soc.*, 1985, **107**, 4964.
22 N. J. Turro, C. A. Renner, W. H. Waddell and T. J. Katz, *J. Am. Chem. Soc.*, 1976, **98**, 4320; M. H. Chang and D. A. Dougherty, *J. Am. Chem. Soc.*, 1982, **104**, 2333.
23 A. J. F. Edmunds and C. J. Samuel, *J. Chem. Soc., Perkin Trans. 1*, 1989, 1267.
24 W. Adam, T. Oppenlander and G. Zang, *J. Org. Chem.*, 1985, **50**, 3303.
25 C. J. Samuel, *J. Mol. Struct. (THEOCHEM)*, 1992, **261**, 115.
26 L. Salem and C. Rowland, *Angew. Chem., Int. Ed. Engl.*, 1972, **11**, 92; see also V. Bonacic-Koutecky, J. Koutecky and J. Michl, *Angew. Chem., Int. Ed. Engl.*, 1987, **26**, 170.
27 R. Hoffmann, A. Imamura and W. J. Hehre, *J. Am. Chem. Soc.*, 1968, **90**, 1499; R. Hoffmann, *Acc. Chem. Res.*, 1971, **4**, 1.
28 H. E. Zimmerman and C. W. Carpenter, *J. Org. Chem.*, 1988, **53**, 3298.
29 C. Doubleday, R. N. Camp, H. F. King, J. W. McIver, D. Mullally and M. Page, *J. Am. Chem. Soc.*, 1984, **106**, 447; F. Bernardi, A. Bottoni, M. A. Robb, H. B. Schlegel and G. Tonachini, *J. Am. Chem. Soc.*, 1985, **107**, 2260.
30 D. K. Lewis, D. A. Glenar, B. L. Kalra, J. E. Baldwin and S. J. Cianciosi, *J. Am. Chem. Soc.*, 1987, **109**, 7225.

Paper 2/05844H
Received 2*nd November* 1992
Accepted 13*th December* 1992