MM2 Force Field Parameters for Compounds Containing the Diazoketone Function

Jonathan M. Goodman,[a] **Jeffrey J. James**[b] **and Andrew Whiting** *,[b]
[a] *Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge UK CB2 1EW*
[b] *Department of Chemistry, UMIST, PO Box 88, Manchester UK M60 1QD*

Force field parameters for use in MM2 modelling programs have been developed for the diazoketone function, from a combination of X-ray crystallographic data, IR spectroscopy, and *ab initio* and semi-empirical calculations. These parameters have been applied to study the accessible conformations and structure of two diazoketone containing molecules, for which X-ray crystallographic data is available. Comparison of X-ray data and calculated geometry was only possible after allowance was made for the effect of crystal packing forces.

The investigation and understanding of the relative stereochemical arrangements of different groups in organic molecules has been greatly assisted in recent years by molecular mechanics calculations.[1] Following some unexpected reactions involving some α-carbonyl diazoketone compounds that required further explanation, we wanted to carry out molecular mechanics calculations on some diazoketone containing structures. Herein, we report the MM2 parameterisation of the diazoketone moiety for use with the MacroModel[2] program, using data derived from X-ray data, IR spectroscopy and *ab initio*[3] and semi-empirical calculations[4] using the methods described by Allinger and co-workers.[1,5]

Force Field Parameters

Crystallographic Data (*Average Bond Lengths and Angles*).—Upon examination of the Cambridge Crystallographic Database[6] using the Crystal Structure Search and Retrieval database (CSSR)† we found several X-ray structures[7–13] which contained the diazo and diazoketone moiety (Table 1). From this data we calculated average bond lengths for the N–N and C–N bonds (*i.e.* bonds *a* and *b*, annotated on structure **8**). Similarly, average bond angles for X–C–C and C–N–N (*i.e.* annotated on structure **8** as θ^1 and θ^2, respectively) were estimated. Remarkably little variance in these bond angles and lengths occurs, even with quite varied functionality around the diazo moiety. In fact, even diazomethane is similar (a = 1.12, b = 1.32 Å).[14]

The average bond lengths and angles are shown in Table 1. The bond angle values were entered into the MacroModel force field, with the C=N=N (θ^1) bond angle assigned as 180° (from 178.41°). The bond length values were compared with those obtained from *ab initio* and semi-empirical calculations before using these values directly (*vide infra*), since X-ray crystallographic data tends to give bond lengths which are longer than those required for the MM2 force field.[5]

Ab initio *Calculations* (*Bond Lengths*).—*Ab initio* calculations were carried out on a simple diazoketone-containing model, *i.e.* structure **9** (see Table 3). This structure was chosen as a suitable model because, when examined by semi-empirical calculations and compared with more complex structures, it adequately represented the diazoketone function (*vide infra*). Full geometry optimisation using the 6–31G* basis set gave bond lengths for the diazoketone and carbonyl functions. The diazoketone bonds (*a* and *b* in **8**) were shorter than the corresponding X-ray data by only 1–2% (Table 2); however, the *ab initio* values were chosen for entry into the force field after a correction factor of 0.004 Å was added.[5b]

Vibrational Data (*Force Constant Calculations*).—The bond stretching parameters were estimated using IR spectroscopic data. Diazoketones are reported to stretch in the regions ~ 1350 (symmetric stretch) and 2010–2180 cm^{-1} (asymmetric stretch).[15] Therefore applying eqns. (1) and (2), where K_s = force constant

$$K_s(\text{symm}) = 5.3 \times 10^{-7} \times \nu^2 \times \mu_{\text{symm}}$$
$$[\mu_{\text{symm}} = (M_1^{-1} - M_2^{-1} + M_3^{-1})^{-1}] \quad (1)$$

$$K_s(\text{asymm}) = 5.3 \times 10^{-7} \times \nu^2 \times \mu_{\text{asymm}}$$
$$[\mu_{\text{asymm}} = (M_1^{-1} + M_2^{-1} + M_3^{-1})^{-1}] \quad (2)$$

(mdyn Å^{-1}),‡ ν = IR stretching frequency (cm^{-1}) and M_n = relative atomic mass of atom n of the triatomic unit, we estimated the force constant for the whole diazoketone group to be 11.590 and 10.280 mdyn Å^{-1} for the symmetric and asymmetric stretches, respectively (assuming that the diazoketone behaves like a linear triatomic molecule). The total stretching constant K_s [average of K_s(symm) and K_s(asymm) = 10.935 mdyn Å^{-1}] is due, in part, to the combined effects of the C–N and N–N stretches. In order to assign the relative combination of each component to the overall stretching constant, we carried out PM3 calculations on a series of diazoketones with a conjugated carbonyl group (*vide infra*). These calculations suggested a contribution of approximately 30% C–N and 70% N–N stretch to the overall (mean) stretching constant calculated from experiment. Thus, splitting the combined stretching constant between C–N and N–N bonds provides K_s(C–N) to be 6.561 and K_s(N–N) 15.309 mdyn Å^{-1}. These figures compare favourably with those calculated using normal modes analysis[17] of IR and Raman spectroscopic data for a single α-diazoketone [K_s(N–N) = 14.0 and K_s(C–N) = 8.9 mdyn Å^{-1}][17a] and an α-diazonitrile [K_s(N–N) = 17.6 and K_s(C–N) = 7.3 mdyn Å^{-1}].[17b] Angle bending parameters were added to the substructure force field based upon existing parameters for groups containing an sp^2 hybridised nitrogen from the MM2 force field in MacroModel.

Van der Waals Parameters (*Non-bonded Interactions*).—The initial selection of the van der Waals parameters was based upon the values already used for nitrogen and carbon in the MacroModel version of the MM2 force field. The values chosen

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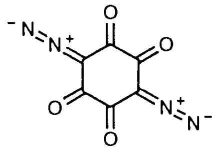
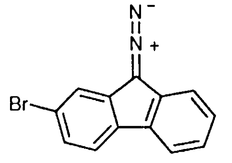
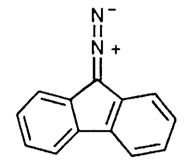
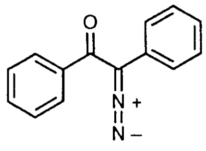
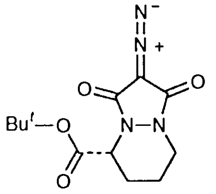
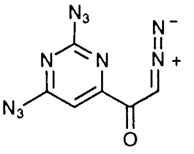
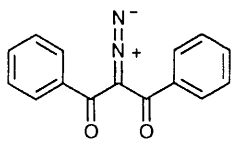
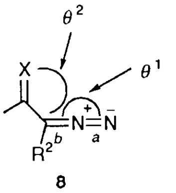
† CSSR was accessed using the database located at the SERC Daresbury Laboratory, Cheshire.

‡ Non-SI unit employed; 1 dyn = 10^{-5} N.

Table 1 Structural data

Structure	Bond lengths/Å	Bond angles/°	Ref.
 **1**	$a = 1.1064$ $b = 1.3567$	$\theta^1 = 177.9$ $\theta^2 = 123.8$	7
 **2**	$a = 1.1253$ $b = 1.3237$	$\theta^1 = 178.4$ $\theta^2 = 120.6$	8
 **3**	$a = 1.1240$ $b = 1.3258$	$\theta^1 = 179.6$ $\theta^2 = 106.3$	9
 **4**	$a = 1.1315$ $b = 1.3251$	$\theta^1 = 177.5$ $\theta^2 = 121.0$	10
 **5**	$a = 1.1188$ $b = 1.2964$	$\theta^1 = 179.3$ $\theta^2 = 130.5$	11
 **6**	$a = 1.1138$ $b = 1.3191$	$\theta^1 = 177.8$ $\theta^2 = 123.7$	12
 **7**	$a = 1.1130$ $b = 1.3380$	$\theta^1 = 175.8$ $\theta^2 = 116.4$	13
 **8**	Average parameters $a = 1.1189$ Å $b = 1.3263$ Å $\theta^1 = 178.04°$ $\theta^2 = 120.32°$		

are identical for all nitrogen types already parameterised in the MM2 force field and proved to reproduce all the structures we have so far examined with reasonable accuracy and hence have remained unchanged in the final force field (*vide infra*). The van der Waals values added were therefore 1.8200 (0.0550) Å (ε)† for the N0 atom type in the N–N–C moiety of the diazoketone itself.

Table 2

Bond	6-31G* Length[a]	Exp. lengths (average)[b]	Force field length[c]
N=N	1.1010	1.1189	1.1050
C=N	1.3096	1.3263	1.3136
C–C	1.4459	1.4300	1.4499
C=O	1.1945	1.2250	1.1985

[a] Average bond lengths of the s-*cis* and s-*trans* conformations of **9**. [b] X-ray determined average bond lengths (see text). [c] Corrected (see ref. 5*b*) average *ab initio* calculated bond lengths.

Semi-empirical and Point Energy Calculations (Torsional Parameters).—Semi-empirical calculations were carried out on a series of general diazoketone containing structures, shown in Table 3. Since the X-ray crystallographic data had demonstrated that the bond angles and lengths for a series of diazoketones were remarkably similar, we needed to ascertain whether there were any significant differences between different calculated structures, before undertaking point energy calculations using PM3.

From the results of these calculations, summarised in Table 3, we found that PM3 calculations reproduce the basic structural features (from X-ray crystallography and *ab initio* calculations) of the diazoketones reasonably well. The only exception is the dicarbonyl **10**, which shows a rather low N=C–C=O (θ^1) dihedral angle, despite the remaining parameters being consistent with the other diazoketone structures (Table 3). For these reasons, we used PM3 calculations and chose the simplest structure **9** as representative diazoketone for the purpose of the point energy calculations in order to estimate the torsional parameters V_1, V_2 and V_3.

Calculation[18] of the torsional parameters was achieved using the truncated Fourier expansion (3).[19] The torsional parameters were estimated from the difference in the calculated torsional parameters found using PM3 and those from MM2.

$$E_{\text{torsion}} = V_1/2(1 + \cos\theta) + V_2/2(1 - \cos 2\theta) + V_3/2(1 + \cos 3\theta) \quad (3)$$

Energy differences were estimated from PM3 point energies for **9** and the MM2 point energies for **9** at 30° intervals of θ, with torsional parameters set to zero in the MM2 force field (Table 4). The resulting values for V_1, V_2 and V_3, estimated using this method (as shown in Table 5), were then added to the MM2 force field. It is interesting to note that the PM3 point energies in Table 3 are not completely symmetric as they should be for a linear, planar group, so the diazo group must be twisting slightly.

Torsional terms have also been added for the N=N=C–C and N=N=C–00 (where 00 is an unspecified atom type). In order to maintain planarity of the central N=C bond, V_2 was given the high value of 10 mdyn Å^{-1} with V_1 and V_3 equal to zero. The final addition to the force field involves two lines for torsional terms which are set to zero, and are necessary to ensure that torsional parameters are not taken from the main field when the diazoketone substructure is used. These are for N=C–C–00 and N=C–00–00 torsions. Similarly, since the effect of lone pairs has been minimised in the new force field, a line for the Lp–N=N=C torsion has been added to ensure that alternative torsional values are not used.

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† Values for the radius (Å) and ε (kcal mol^{-1}) were taken from the main MM2 force field as used in MacroModel (see ref. 2) and are used in a standard Lennard-Jones equation for the calculation of the van der Waals energy: see ref. 2 (Appendix A).

Table 3

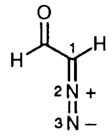
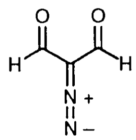
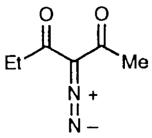
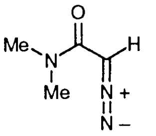
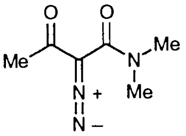
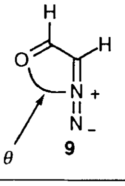
Structure	Bond lengths/Å	Bond angles	Partial Charges
 **9**	a = 1.1297 b = 1.3124	θ^1 = 179.96 θ^2 = 121.65	C_1 −0.6984 N_2 +0.7666 N_3 −0.3449
 **10**	a = 1.1655 b = 1.4050	θ^1 = 136.98 θ^2 = 126.47	C_1 −0.7029 N_2 +0.4002 N_3 −0.5119
 **11**	a = 1.1330 b = 1.2808	θ^1 = 177.60 θ^2 = 119.61	C_1 −0.6939 N_2 +0.7933 N_3 −0.3054
 **12**	a = 1.1272 b = 1.3171	θ^1 = 178.22 θ^2 = 123.66	C_1 − 0.6558 N_2 +0.7953 N_3 −0.3329
 **13**	a = 1.1330 b = 1.2808	θ^1 = 175.74 θ^2 = 119.63	C_1 −0.6608 N_2 +0.7868 N_3 −0.2965

Table 4



9

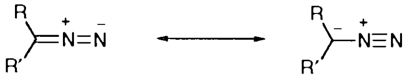
θ/°	PM3 energy /kcal mol^{-1}	MM2 energy /kcal mol^{-1}
0	0	0
30	1.9082	0.2414
60	6.1648	1.0182
90	8.9723	2.6195
120	7.9749	0.9943
150	5.2184	0.2462
180	3.8834	0.0191
−150	5.2274	0.2462
−120	7.9913	0.9943
−90	9.0085	2.6195
−60	6.2204	1.0182
−30	1.9518	0.2414

Table 5 Torsional parameters

	V_1/kcal mol^{-1}	V_2/kcal mol^{-1}	V_3/kcal mol^{-1}
PM3	−3.7920	7.0400	−0.1010
MM2	0.0580	2.1890	0.0370
($V^{PM3} - V^{MM2}$)	−3.8500	4.8510	−0.1380

Lone Pair and Partial Charge Parameters.—The final approximation made in the new force field has been to make some allowance for the lone pairs and partial charges of the diazoketone. As an initial approximation to the behaviour of the diazoketone, we have assumed that atom-centred partial charges alone satisfactorily model this group. Since the MultiConformer subroutine[20a] of MacroModel, which was used to check the reliability of the force field (*vide infra*), does require lone pairs to be present in order for the substructure to be recognised, we have added lines to the force field relating to the lone pairs but reduced their impact on the energy calculations effectively to zero by reducing the effective size of the lone pairs to 0.0010 Å, with the force constant being that for an sp^2 hybridised nitrogen in the MM2 force field of MacroModel.

Viewed in a classical sense, the diazoketone moiety may exist in two possible canonical forms, **14a** or **b**. However, it is likely that neither of these forms fully reflects the real electronic structure of the diazoketone and the electronics are better mirrored by a mixture of the two forms. The PM3 calculations reported in Table 3 also included calculated partial charges for the C-N-N moiety of structure **9** and we compared these charges with the partial charges calculated from the *ab initio* calculations (*vide supra*).



14a **14b**

The PM3 calculations gave rather large Mulliken charges (−0.6984, +0.7666 and −0.3449 for the C-N-N atoms of the diazoketone respectively) for **9**, when compared with the *ab initio* calculated charges for the same molecule (−0.2437, +0.1355 and −0.1266 for the same atoms). The *ab initio* calculated charges for structure **9** were added to the force field, after suitable scaling.[21]

Force Field.—All these parameters were added to the MM2 force field of MacroModel, creating a substructure force field which is shown in Table 6.

Molecular Mechanics Calculations

In order to determine whether the force field described by Table 6 could be used to accurately reproduce the structural features of the diazoketone function, we undertook molecular mechanics calculations on the simple diazoketones shown in Table 3 by using both the Multi-Conformer and Monte Carlo[20] conformational search subroutines in MacroModel. The most interesting example examined from Table 3 was **9**, since this compound had been studied by both *ab initio* and semi-empirical methods (*vide supra*). A conformational search on **9** revealed only two conformations (the s-*cis* and s-*trans* structures **9a** and **b** respectively) using either Multi-Conformer or Monte Carlo, which differed by only 0.32 kcal mol^{-1} † in energy. The results for the molecular mechanics calculations on **9** are summarised in Table 7. From this Table, it can be seen that the force field parameters reproduce closely the expected bond lengths and angles calculated by both *ab initio* and semi-empirical methods for structures **9**, with the difference in energy between conformations being closest to the *ab initio* calculated value. Also of note is the fact that all methods predict only two conformations for **9**, which is perhaps expected if the diazoketone is considered as behaving in a similar manner to buta-1,3-dienes, unsaturated aldehydes and related structures.[22-25] Finding the s-*cis* conformation to be more stable than the s-*trans* conformation was also not entirely unexpected. NMR experiments have shown[26] that the s-*cis* conformations of a wide range of diazoketones are very much preferred. For example, in solution, **9** exists as an approximately 7:3 mixture of s-*cis*:s-*trans* rotamers [the gas phase calculated ratio for these two conformations, using an energy difference of 1.33 kcal mol^{-1} (Table 7), is approximately 9:1], but if the aldehyde group is replaced by an alkyl (methyl or ethyl), the s-*cis* conformation is favoured even more (approximately 9:1). In comparison, phenone-derived simple diazoketones exist as single rotamers in solution and are thought[26] to have the s-*cis* arrangement of the carbonyl to the diazo function. This preference for the s-*cis* arrangement may be an important factor in certain reactions of diazoketones, such as the Wolff rearrangement.[26]

The origin of the preference for the s-*cis* versus s-*trans* conformations of diazoketones has been interpreted in terms of a substantially steric effect; however, electronic effects are also likely to have a profound effect upon such a polar function. In order to probe this further, we calculated the energy of the accessible conformations of several related conjugated systems (see Table 8) using the MM2 force field of MacroModel and compared these values with any relevant experimental data. As expected,[22-25] the s-*trans* conformations for most of the conjugated systems are predicted to be the most stable, except when the conjugated iminium ions were examined. In both the iminium ion cases examined (Table 8), the s-*cis* conformations were preferred (as with diazoketone **9**), hence the slightly greater stability of the s-*cis versus* s-*trans* conformation for the diazoketone **9** can be interpreted by the effect of the attraction of

Table 6 MM2 Parameters for diazoketone substructure

Main field: van der Waals interactions for unspecified nitrogen (N0)							
N0	1.8200				0.0550	0.0000	0000 A3
Substructure: α-diazoketone carbonyl moiety							
C	Diazo group						
9	N0=N0=C2–C2=O2						
−2							
1	1	2			1.1084	15.3090	
1	2	3			1.3088	6.5610	
1	3	4			1.4527	6.0000	
1	4	5			1.1962	5.0000	
1	Lp	1			0.0010	6.1000	
2	1	2	3		180.0000	0.4300	
2	2	3	4		120.9800	0.6900	
2	2	3	00		120.0000	0.5000	
2	3	4	5		120.0000	0.4600	
2	Lp	1	2		128.5000	0.3500	
2	Lp	1	Lp		120.0000	0.5000	
4	1	2	3	4	0.0000	10.0000	0.0000
4	1	2	3	00	0.0000	10.0000	0.0000
4	2	3	4	5	−3.8500	4.8510	−0.1380
4	2	3	00	00	0.0000	0.0000	0.0000
4	2	3	4	00	0.0000	0.0000	0.0000
4	Lp	1	2	3	0.0000	0.0000	0.0000
−4							
8	−0.1152	0.1233			−0.2218	0.3033	−0.4735

Table 7 Bond lengths and angles calculated for diazoketone **9**

	MM2		PM3		*ab initio*	
	9a	**9b**	**9a**	**9b**	**9a**	**9b**
Bond lengths/Å						
1–2	1.186	1.187	1.215	1.211	1.197	1.192
2–3	1.454	1.454	1.456	1.464	1.443	1.449
3–4	1.316	1.316	1.319	1.313	1.314	1.305
4–5	1.111	1.111	1.127	1.130	1.098	1.104
Bond angles/°						
1–2–3	122.6	122.5	123.7	121.7	124.9	123.7
2–3–4	120.3	120.4	122.7	122.5	117.0	118.3
3–4–5	180.0	179.9	178.9	180.0	180.0	180.0
Torsion angle/°						
1–2–3–4	0.0	180.0	−0.2	179.9	0.0	180.0
Energy difference [(s-*trans*) − (s-*cis*)]/kcal mol^{-1}						
	−1.33		−3.05		−1.32	

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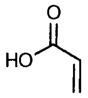
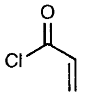
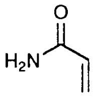
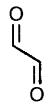
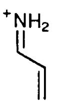
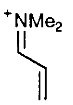
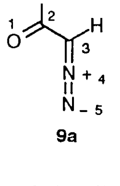
† 1 cal = 4.184 J.

Table 8 MM2 calculated *versus* experimental energy differences (kcal mol^{-1}) (most stable conformation) between s-*cis* and s-*trans* conformations [(s-*trans*) − (s-*cis*)]

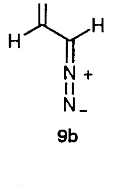
Structure	MM2	Experiment
	2.6 (s-*trans*)	2.3[a] (s-*trans*)
	1.6 (s-*trans*)	1.7–2.0[b] (s-*trans*)
	0.1 (s-*trans*)	—
	0.9 (s-*trans*)	0.3–0.6[c] (s-*trans*)
	0.8 (s-*trans*)	—
	2.4 (s-*trans*)	3.2[d] (s-*trans*)
	7.5 (s-*cis*)	—
	4.9 (s-*cis*)	—

[a] See ref. 22. [b] See refs. 22 and 23. [c] See refs. 23 and 24. [d] See ref. 26.

the charge on the oxygen carbonyl to the central nitrogen of the diazoketone. This interpretation of the effect of the coulombic attraction of the carbonyl oxygen to the central nitrogen atom of the diazoketone is also supported by spectroscopic and dipole moment evidence from related structures,[27] and was borne out by removing the charge on the central nitrogen from the force field followed by rerunning the conformational search on **9**. The result of this calculation was a reversal in the relative stability of the s-*cis* and s-*trans* conformations.



9a



9b

The utility of the diazoketone force field was tested using compounds for which X-ray crystallographic data was available from the Cambridge Crystallographic Database,[6] particularly molecules **4**[10] and **7**[13]. For these compounds X-ray crystallographic data was available,[10,13] and some structural information was also available.[27] There has been considerable discussion in recent years about the different methods that are available for searching the conformational space of organic molecules.[28,29] Molecules **4** and **7** do not have a large number of rotatable torsion angles, but they could possess a large number of low energy conformations due to (*a*) neighbouring groups which are relatively highly polarised and (*b*) sterically demanding groups in close proximity to each other.

Before undertaking full conformational searches on **4** and **7**, we needed to estimate the effects crystal packing forces on the X-ray structures of **4** and **7** since the conformational search calculations would be gas-phase calculations and the structures thus generated would not be expected to be directly comparable. To be able to achieve a more direct comparison, we carried out experiments to estimate the approximate energetic effect of crystal packing upon an isolated molecule, using the starting X-ray structures of **4** and **7** (as discussed by Allinger †). The method we used to do this was firstly to constrain the non-hydrogen atoms of the structures to their X-ray positions (effectively placing them in isolation in the gas-phase) and minimise the structures using the MM2 force field, to optimise the hydrogen positions in the X-ray structures and produce an estimate of the relative potential energy of the actual X-ray structures as though they were in the gas phase. Secondly, to minimise the fully unconstrained X-ray structures using the MM2 force field, thus estimating the relative potential energy of the structures' most closely related minima to those of the actual X-ray structures of **4** and **7**. Thirdly, to compare the results of the structures generated from the constrained and unconstrained calculations above to estimate the relative potential energy required to deform each structure into the crystal. The results of this exercise are summarised in Tables 9 and 10.

The most noteworthy aspects of these results are that for both structures **4** and **7**, only slight changes occur in the structures upon constrained minimisation. However, when compared with the unconstrained structures, it is clear that considerable strain has been imposed upon the structures in order to achieve crystal packing, not in terms of bond lengths and angles, but in terms of dihedral angles and in particular the diazoketone-carbonyl ones. For **4** (Table 9), the O–C–C–N dihedral angle changes by 100° upon minimisation, taking the structure from an approximately s-*trans* arrangement to a nearly s-*cis* arrangement. The calculated potential energy for the constrained structure **4** was found to be 16.74 kcal mol^{-1}, *versus* 8.74 kcal mol^{-1} for the unconstrained structure, giving an estimated energy due to constraint in the crystal of a single molecule of 8.00 kcal mol^{-1}.

A similar result was obtained for **7** (Table 10). One of the diazoketone-carbonyl dihedral bonds changes by 22° upon minimisation, but still retains a very approximately s-*trans* arrangement. This smaller change in dihedral angle was also reflected in the energy due to constraint in the crystal for **7**. The constrained structure had a potential energy of 11.29 *versus* 5.49 kcal mol^{-1} for the unconstrained structure, a constraining energy of 5.80 kcal mol^{-1}. Therefore, in both cases, the diazoketones are compressed into a more planar arrangement in the crystal than the gas-phase molecules would prefer. The fact that less substituted diazoketones prefer to have a co-planar arrangement of the diazoketone and carbonyl groups shows the severe effects of non-bonded steric repulsions in **4** and **7**.

Having investigated the structures of **4** and **7** which are based on the X-ray structures, we undertook the searching of the conformational space of structures **4** and **7** to see if the gas-phase calculated structures were closely related to the global minima for both **4** and **7**. This was achieved by selecting all

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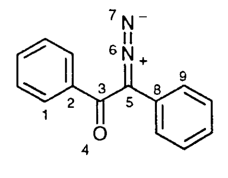
† For a discussion of applications of calculations to estimate the effects of crystal packing upon individual molecules, see ref. 4(*c*), p. 307.

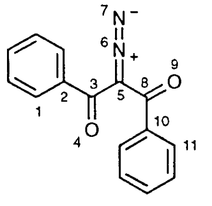
Table 9



4

Structure **4**	X-Ray	Constrained minimised X-ray	Unconstrained minimised X-ray
Bond lengths/Å			
2–3	1.492	1.490	1.489
3–4	1.232	1.225	1.219
3–5	1.457	1.464	1.457
5–6	1.325	1.317	1.312
6–7	1.131	1.111	1.109
5–8	1.483	1.478	1.471
Bond angles/°			
2–3–4	119.3	119.1	123.6
4–3–5	121.0	122.1	117.5
3–5–6	115.6	117.0	118.8
5–6–7	117.5	178.4	179.7
6–5–8	116.0	116.6	120.8
Dihedral angles/°			
1–2–3–4	40.1	39.3	−4.8
4–3–5–6	−165.1	−163.0	−60.4
6–5–8–9	−18.3	−19.0	−40.7

Table 10



7

Structure **7**	X-Ray	Constrained minimised X-ray	Unconstrained minimised X-ray
Bond lengths/Å			
2–3	1.486	1.492	1.490
3–4	1.222	1.223	1.221
3–5	1.472	1.469	1.457
5–6	1.337	1.318	1.313
6–7	1.113	1.109	1.109
5–8	1.477	1.466	1.457
8–9	1.221	1.246	1.245
8–10	1.486	1.480	1.489
Bond angles/°			
2–3–4	121.6	120.9	122.9
4–3–5	120.1	121.3	117.8
3–5–6	116.4	117.6	119.0
5–6–7	175.8	176.6	179.5
6–5–8	111.4	112.6	118.6
5–8–9	119.8	118.7	117.6
9–8–10	121.2	120.1	122.9
Dihedral angles/°			
1–2–3–4	−28.4	−27.5	−6.9
4–3–5–6	143.3	141.6	119.8
6–5–8–9	−9.9	−10.3	−36.3
9–8–10–11	−28.4	−27.7	−8.7

the single bond torsions on the fully minimised structures and carrying out both MultiConformer†[20a] and Monte Carlo [using the Systematic, Unbounded Multiple Minimum option (SUMM)][20b,30] searches.

Once a set of conformations had been generated using the Monte Carlo search, we examined each of the structures with particular attention to the dihedral angles. The structures generated from the searches were all fully converged (energy gradients < 0.01) and were all minima, not saddle points, as confirmed by calculation of vibrational frequencies. For **4**, there were only two conformations found (Table 11), but for **7**, three conformations exist. However, the third conformation was the enantiomer of the second by virtue of limited rotation about the central bonds, *i.e.* they were atropisomers. Thus, the two conformations (excluding the enantiomer of conformation 2 found for **7**) are shown in Table 11. The global energy minimum conformations found for both **4** and **7** are shown in Table 11 (conformations 1), together with the next lowest minimum (conformations 2) and their corresponding dihedral angles and energies. The MultiConformer subroutine gave the same low energy structures as the Monte Carlo search.

From the structures shown in Table 11, both **4** and **7**, the diazoketones, are unable to exist in a completely planar arrangement with the carbonyl groups, but the low energy conformations show that the structures do try to adopt conformations in which the diazoketone gets as close to being in-plane with the carbonyl as possible while avoiding severe non-bonded interactions with the phenyl rings. This point is reinforced by the finding of atropisomers for **7**. The competing effects of the drive for planarity *versus* steric repulsion results, in the case of **4**, in atoms 4–3–5–6 (N–C–C–O) adopting dihedral angles of 60.2° and 102.0° which are the nearest approximations to an s-*cis* and an s-*trans* arrangement, respectively, that the molecule can adopt.

A similar result occurs with **7**. Complete planarity between the diazoketone and the carbonyl groups is impossible, again due to severe steric repulsion between the *ortho*-hydrogens on the phenyls and the carbonyl lone pairs. For **7**, the balance is found by adopting two low energy conformations which approximate to s-*trans*, s-*trans* (conformation 1) and s-*cis*, s-*trans* (conformation 2) arrangements. This conclusion is supported by the results from ^{13}C NMR, IR and dipole moment studies[27] on **7**, which suggested that at least two low energy conformations exist in equilibrium at room temperature in solution [which were termed (*E*,*E*)- and (*E*,*Z*)-conformations, *i.e.* s-*trans*, s-*trans* and s-*cis*, s-*trans* conformations] and these two conformations have reduced double bond character between the diazoketone and carbonyl groups, as evidenced by the IR stretches. Our calculations similarly suggest that two conformations exist in equilibrium and each would possess diminished diazoketone-carbonyl orbital overlap, with the approximately s-*trans*, s-*trans* conformation being lower in energy in the gas phase, but only by 0.68 kcal mol^{-1}.

We have parameterised the diazoketone group for use with the MM2 force field of MacroModel. These parameters were devised using data from X-ray crystallography and IR spectroscopy, supplemented by *ab initio* calculations, using the 6–31G* basis set, and semi-empirical calculations, using the

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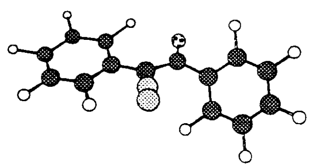
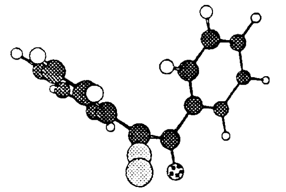
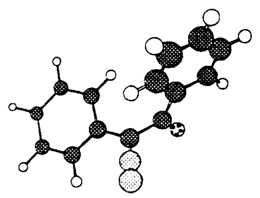
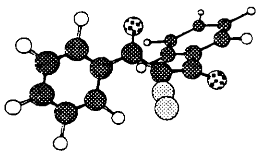
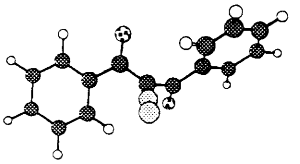
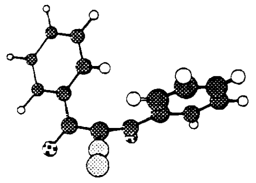
† For MultiConformer searches, all C–C single bond torsions were allowed to rotate with 60° resolution, and 10° resolution for bond angles. PRCG minimisation was chosen, with an energy window of 150 kJ mol^{-1}.

Table 11

Structure 4: X-ray and two lowest energy conformations.					
					
X-ray		Conf. 1; 8.74 kcal mol^{-1}		Conf. 2; 9.05 kcal mol^{-1}	
Dihedral angles:					
1-2-3-4	40.1	1-2-3-4	4.8	1-2-3-4	-1.9
4-3-5-6	-165.1	4-3-5-6	60.2	4-3-5-6	102.0
6-5-8-9	-18.3	6-5-8-9	40.6	6-5-8-9	-24.1
Structure 7: X-ray and two lowest energy conformations.					
					
X-ray		Conf. 1; 4.81 kcal mol^{-1}		Conf. 2; 5.49 kcal mol^{-1}	
Dihedral angles:					
1-2-3-4	-28.4	1-2-3-4	1.0	1-2-3-4	6.9
4-3-5-6	143.3	4-3-5-6	-101.7	4-3-5-6	-119.0
6-5-8-9	-9.9	6-5-8-9	-101.7	6-5-8-9	37.2
9-8-10-11	-28.4	9-8-10-11	1.0	9-8-10-11	8.6

PM3 Hamiltonian. The new parameters have to be used to carry out molecular mechanics calculations on simple diazoketones and give good structural results when compared with structures derived from *ab initio* and semi-empirical methods. The new parameters will be used to address an intriguing problem relating to axial chirality in a diazoketone containing molecule.[31]

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