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THEORETICAL STUDY ON STRUCTURES AND INTERNAL ROTATIONS OF METHYL *N,N*-DIMETHYLCARBAMATE AND ITS SULPHUR, SELENIUM, AND TELLURIUM HOMOLOGUES ($Me_2NC(O)YMe$, Y = O, S, Se, Te)

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A theoretical study on the structures and internal rotations of methyl *N,N*-dimethylcarbamate and its sulphur, selenium and tellurium homologues [$Me_2NC(O)YMe$, 1 (Y = O), 2 (Y = S), 3 (Y = Se), 4 (Y = Te)] was performed by means of *ab initio* molecular orbital calculations at the MP2/3-21G(*)//HF/3-21G(*) level. These calculations indicate that 1–4 are all planar with *Z*-conformation with respect to the central bonds of their O=C—Y—Me units, whereas the corresponding *E*-forms are transition states for rotation about Y—C(O) bonds which have energies higher than the *E*-forms by 20·6, 15·4, 13·9, and 9·6 kcal mol^{-1}, respectively. The energy of 1 increases monotonically from the *Z*-form to the *E*-form with rotation about the Y—C(O) bond, but in 2–4 a transition state and a local minimum were found between the two forms. This different phenomenon for 1 compared with its homologues 2–4 arise mainly from the large steric repulsion between a methyl group on the nitrogen and that on the oxygen in *E*-1. Optimization of the transition states (TS_a and TS_s) for rotation about N—C(O) bonds showed that TS_a is favoured by 2–4 but disfavoured by 1 owing to the repulsion between lone pairs on the nitrogen and oxygen atoms in its TS_a. The barriers for rotation about N—C(O) bonds were estimated to be 16·1, 14·7, 14·7, and 15·7 kcal mol^{-1} for 1, 2, 3, 4, respectively.

INTRODUCTION

Heteroatomic compounds have been widely employed as important reagents in modern synthetic reactions, allowing novel transformations with the aid of the characteristic chemical properties of the heteroatoms. In the course of our studies on the chemistry of chalcogen elements, we have developed unique preparative methods for thio-,[1] seleno-[2] and tellurocarbamates[3] and also demonstrated the potent synthetic utility of tellurocarbamates as nucleophilic carbamoylation reagents.[3b,c] In this paper, we report the results of a theoretical study on the structures and conformations of methyl *N,N*-dimethylcarbamate and its sulphur, selenium, and tellurium homologues [$Me_2NC(O)YMe$, **1** (Y = O), **2** (Y = S), **3** (Y = Se), **4** (Y = Te)].

As related compounds to carbamates, amides have attracted much attention from their conformational aspects inasmuch as they serve as prototypes of important polypeptides and proteins.[4] Many experimental and theoretical studies on amides have shown that they are planar or very close to planar.[5–7] This phenomenon has been explained by the conjugation between the carbonyl group and the nitrogen.[5] However, recent theoretical calculations revealed that the rotation about N—C(O) bonds causes little change in the C=O bonding, suggesting that such a resonance contribution may not be important.[8,9]

Esters have two stable planar structures, i.e. *E*- and *Z*-forms with respect to the central bond of the O=C—O—R unit.[5] In contrast to amides, it is difficult to measure the rotational barrier or energy difference between these two forms since the equilibrium is generally biased far to the *Z*-form. However, for some simple compounds, *E*–*Z* energy differences and barriers between them have been estimated experimentally[10] and theoretically,[11] showing for example that *Z*-forms are more stable than the others by about 3·9[10a] or 4·8[10b] kcal mol^{-1} (1 kcal = 4·184 kJ) for methyl formate and about 8·5 kcal mol^{-1} for methyl acetate[10b,11a] with barriers of *ca* 7–15 kcal mol^{-1}.[10b–d,11a] The *E*–*Z* energy differences decrease appreciably in polar solvents.[11b]

Carbamates, which include both amide and ester frameworks, are also important compounds since the

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NCO_2 skeleton often appears in bioactive compounds, such as anticonvulsants, local anaesthetics, sedatives, hypnotics and muscle relaxants,[12] and in significant industrial materials such as polyurethanes.[13] However, in contrast to the extensive studies on amides and esters, much less attention has been given to the structures of carbamates.[13,14] X-ray[13a,14a,b] and theoretical[14c-h] studies have shown that carbamate frameworks are also planar or nearly planar. Conformational interest in carbamates is focused mainly on the rotation about their N—C(O) bonds, for which several theoretical[14c-h] and experimental[i-o] data are available, but little attention has been paid to rotation about their O—C(O) bonds. As for their analogues, several thio- and dithiocarbamates, which also have interesting pharmacological activities, such as antibacterial, anticholinergic, antidotal, antifungal, antivirial, herbicidal, local anaesthetic and tuberculostatic activities,[12,15,16] have been studied,[14c,f,j-o] but selenium[14k] and tellurium analogues have scarcely been reported.

COMPUTATIONAL METHOD

Molecular orbital calculations were performed with *ab initio* methods using the theoretical calculation package Spartan Versions. 2.1 and 3.1. (Wavefunction, Irvine, CA, USA) All structures were optimized at the Hartree–Fock level of theory using 3–21G(*) basis sets,[17] since these afford sufficiently reliable structures and energies,[14d] although more accurate values may of course be obtained by calculations at higher levels of theory with larger basis sets.[8,9,18] Structures at stationary points were fully optimized without any constraint and their energies were calculated also with the second-order Møller–Plesset perturbation theory (MP2).[19]

RESULTS AND DISCUSSION

Structures of 1–4

As mentioned above, many studies reported so far on the structure of carbamates, amides and esters indicate that the central framework of $Me_2NC(O)YMe$ is (nearly) planar, having a nitrogen with sp^2 hybridization. As for the geometries of their ester fragments (O3—C2—Y1—C7), both *E*- and *Z*-forms are expected to exist as stable conformers (Figure 1). We therefore first attempted to optimize both forms of **1–4** at the HF/3–21G(*) level, but no energy minima were found for *E*-forms for any of the compounds. However, structure optimization of *E*-forms adopting C_s symmetry afforded transition states with one negative frequency which corresponds to rotation about their Y1—C2 bonds in the case of **2–4** (see below). Similar calculations with **1** gave a structure which had two negative frequencies corresponding to rotations about Y1—C2 and N4—C6 bonds. However, a transition search approach for **1** with *C*1 symmetry afforded a slightly distorted *E*-form as a transition state for Y1—C2 rotation. These phenomena are in great contrast to those of esters, which usually have local minima for *E*-forms.[5,11b]

All the compounds **1–4** have stable *Z*-forms, but small geometrical differences in their optimized struc-

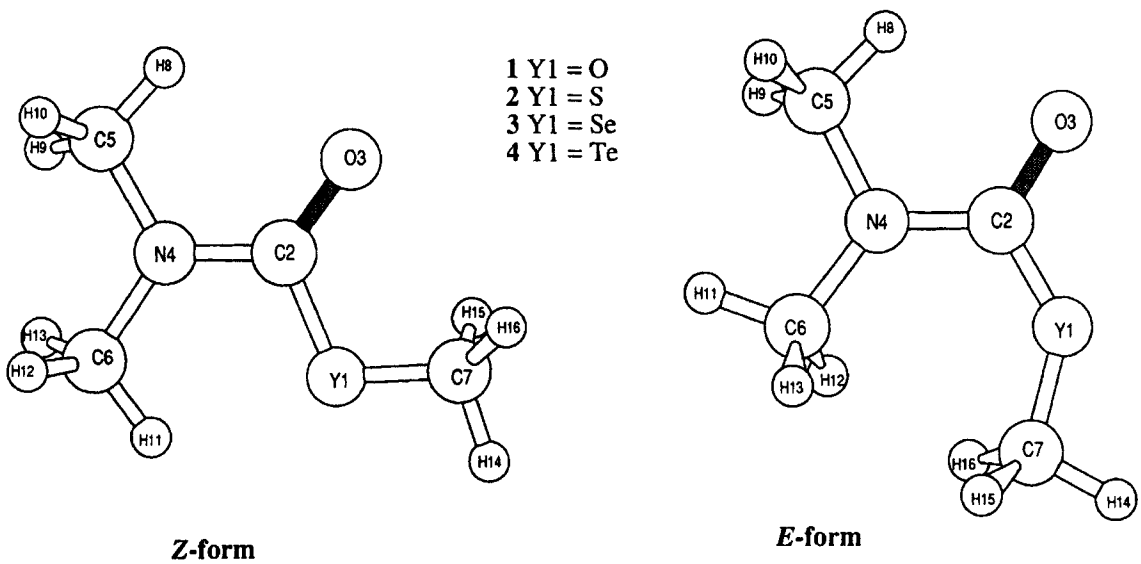


Figure 1. Conformations of *Z*- and *E*-forms of **1–4**

tures were observed between **1** and heavier analogues **2–4**, i.e. (*Z*)–**1** is completely planar whereas the *Z*-forms of **2–4** are slightly distorted, having small dihedral angles of O3—C2—Y1—C7. Optimization of the *Z*-forms of **2–4** adopting C_s symmetry led to saddle points which have a slightly higher energies than the ground states by 0·01, 0·04, and 0·03 kcal mol^{-1}, respectively. However, such deviations from complete planarity in the case of **2–4** may be chemically insignificant since the energy differences are very small.

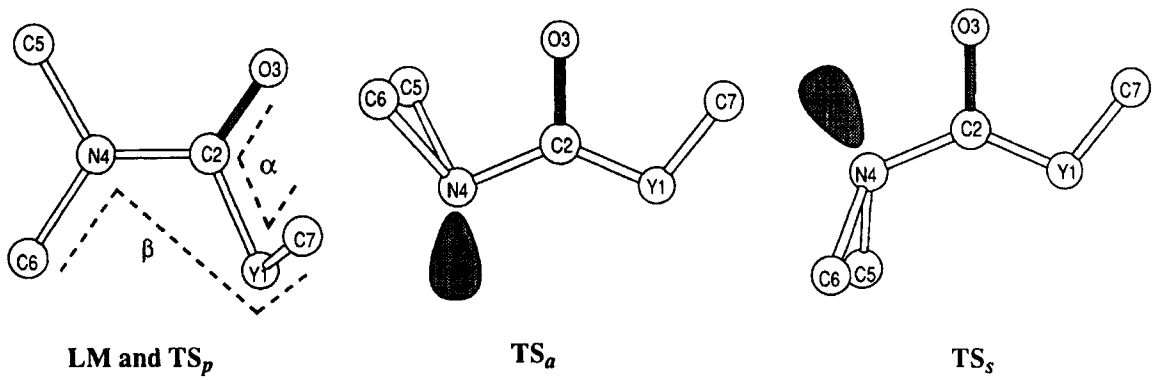
In Table 1 are listed some geometrical parameters of the optimized structures. The structure of (*Z*)–**1** obtained is very close to a reported structure optimized at the HF/6–31G* level[14d] and also to structures of similar compounds determined by x-ray analysis.[13a,14a,b] In the *Z*-forms of **1–4**, the nitrogen atoms are planar and the C5—H8 bonds are (nearly) eclipsed to the C2—N4 bonds. As for the conformation of C6-methyl groups, one C—H bond is eclipsed to the C2—N4 bond in **1**, but is nearly perpendicular in **2–4**.

The *E*-forms are all saddle points, as mentioned above, probably owing to the steric repulsion between a methyl group on N4 and that on Y1. The relative energies of the *E*-forms in comparison with the *Z*-forms are listed in Table 2. The *E*–*Z* energy difference decreases as Y becomes heavier, i.e. 20·6, 15·4, 13·9, and 9·6 kcal mol^{-1} for **1**, **2**, **3** **4**, respectively, which might represent rotational barriers about Y1—C2 bonds (see below).

Rotation about Y1—C2 bonds

In order to reveal the energy profile for the rotation about Y1—C2 bonds, the structures of **1–4** were optimized adopting constrained values for the dihedral angle α defined by O3—C2—Y1—C7 (Figure 2), which was increased step by step from 0° to 180° (up to 210° in the case of **1**). The relative energies of these optimized structures calculated at the Hartree–Fock level are plotted in Figure 3. It is interesting that the energy of **1** increases monotonically (up to *ca* 210° in the local minimum search), whereas **2–4** have transition states (TS_p) with the Y1—C7 bond nearly perpendicular to the molecular plane ($\alpha \approx 95°$) and local minima (LM) with $\alpha = 115{\cdot}6° - 142{\cdot}3°$. The relative energies and selected geometrical parameters of these stationary points are given in Tables 2 and 3, respectively.

Local minima searches with a constrained α of 180° afforded optimized structures having C_1 symmetry which have lower energies than their *E*-forms by 1·5, 0·6, 0·02, and 0·01 kcal mol^{-1} for **1**, **2**, **3**, **4**, respectively, at the Hartree–Fock level. In the cases of **1** and **2**, the optimized structures are appreciably distorted from C_s symmetry. Figure 4 shows the structure of **1** optimized with $\alpha = 180°$ in which the nitrogen loses planarity, probably owing to steric repulsion between a methyl group on N4 and that on O1. The importance of such repulsion is clearly evidenced by comparison with methyl carbamate (**5**, H_2NCO_2Me), for which such repulsion is not expected even in its *E*-form. When similar calculations were performed with **5**, the *E*-form having C_s symmetry became a local minimum (10·7 kcal mol^{-1} higher than the *Z*-form) and a transition state (11·4 kcal mol^{-1} higher than the *Z*-form) was found between the *E*-and *Z*-forms, as shown in Figure 3. This energy profile is very similar to that of O—C(O) rotation of methyl acetate reported recently,[11] where the *Z*-form is preferred over the *E*-form by 9·4 kcal mol^{-1} at the HF/6–31+G** level with a transition state *ca* 13 kcal mol^{-1} higher than the *Z*-form. Evidence that the curve for **5** is almost superimposable on that of **1** within the range of $0° < \alpha < 90°$ indicates that repulsion between these two methyl groups plays an important role when $\alpha > 90°$. Another approach was adopted in order to include this repulsion more naturally in the energy diagram. When the structure of **1** was optimized with a constrained dihedral angle of C6—N4—O1—C7 (β), a very smooth energy profile



LM and TS_p **TS_a** **TS_s**

Figure 2. Conformations of LM, TS_p, TS_s, and TS_a. Hydrogens are omitted for clarity

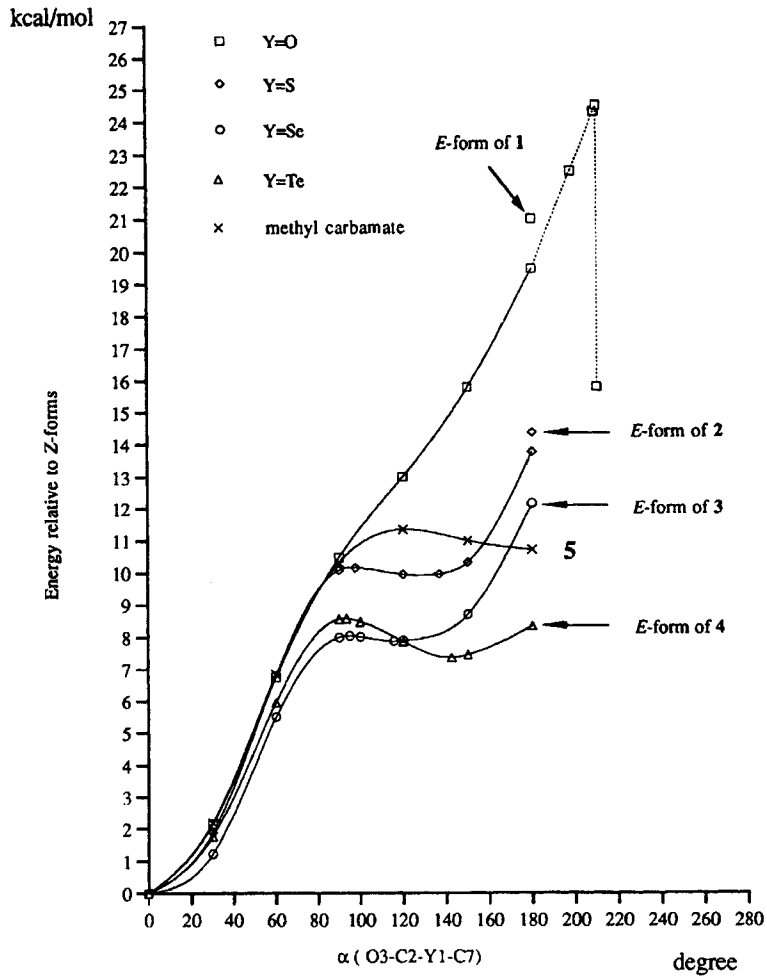


Figure 3. Energy profiles for rotation about Y1—C2 bonds of **1**–**4** and methyl carbamate

from the *E*-form to the *Z*-form was obtained as shown in Figure 5.

The *E*–*Z* energy differences decrease in the order **1**>**2**>**3**>**4**, which is the opposite to the order of the C6—C7 atomic distances of the *E*-forms, i.e. 2·937, 3·056, 3·133, and 3·455 Å, respectively. This may also suggest that repulsion between these two methyl groups is one of the major factors in the *E*–*Z* energy differences.

The transition states (TS_p) of **2** and **3** are apparently more stable than their *E*-forms, and the TS_p of **4** has almost the same energy as the *E*-form, indicating that *E*-forms are transition states for rotation about Y1—C2 bonds. The rotational barrier of 20·6 kcal mol^{-1} obtained for **1** is larger than the corresponding rotational barrier of 7–15 kcal mol^{-1} reported for esters.[10b-d,11a] However, its homologues **2**–**4** have similar barrier heights to those of esters.

Rotation about N4—C2 bonds

It is known that amides have two kinds of transition states for their internal rotation about N—C(O) bonds, i.e. TS_a and TS_s, which have a lone pair on the nitrogen *anti* and *syn* to the carbonyl oxygen, respectively (Figure 2).[9] For **1**–**4**, the structures of TS_a and TS_s were optimized adopting C_s symmetry. Selected structural parameters and relative energies from their *Z*-forms are summarized in Tables 3 and 2, respectively. These calculations showed that **2**, **3**, and **4** preferred TS_a than the other by 3·3, 2·0, and 1·8 kcal mol^{-1}, respectively. Here also **1** is unique from others, i.e. TS_s is more stable

Table 1. Selected structural parameters of *Z*- and *E*-forms of **1**–**4**[a]

Compound	Bond distance (Å)			Bond angles (°)				Dihedral angles					
	C2—Y1	C2—N4	C2—O3	N4—C2—O3	O3—C2—Y1	Y1—C2—N4	C2—Y1—C7	O3—C2—N4—C5	C5—C2—N4—C6	O3—C2—Y1—C7	C2—N4—C5—H8	C2—N4—C6—H11	C2—Y1—C7—H14
(*Z*)-**1**	1·357	1·346	1·217	125·8	121·7	112·5	116·9	0·0	180·0	0·0	0·0	0·0	180·0
(*E*)-**1**	1·357	1·367	1·211	122·4	117·1	120·5	134·8	−0·1	−179·8	180·0	−0·3	179·6	179·8
(*Z*)-**2**	1·796	1·351	1·220	123·6	121·3	115·1	99·3	4·0	173·8	1·5	−6·0	33·5	−2·4
(*E*)-**2**	1·800	1·350	1·221	123·1	110·6	126·3	114·9	0·0	180·0	180·0	0·0	180·0	180·0
(*Z*)-**3**	1·949	1·350	1·218	124·0	120·7	115·3	95·3	3·6	174·8	1·5	−5·4	43·5	−1·5
(*E*)-**3**	1·952	1·347	1·219	123·7	110·0	126·3	113·1	0·0	180·0	180·0	0·0	180·0	180·0
(*Z*)-**4**	2·196	1·350	1·219	123·7	118·0	118·3	90·9	3·4	174·5	1·7	−5·1	27·4	−1·1
(*E*)-**4**	2·191	1·345	1·221	123·8	107·9	128·3	111·1	0·0	180·0	180·0	0·0	180·0	180·0

[a] *E*-Forms were optimized adopting C_s symmetry for **2**–*4* or by a transition search approach with C_1 symmetry for **1**.

Table 2. Relative energies in kcal mol^{-1} calculated at the HF (MP2) level

Structure	1	2	3	4
Z-Form	0 (0)	0 (0)	0 (0)	0 (0)
E-Form	21·0 (20·6)	14·4 (15·4)	12·7 (13·9)	8·4 (9·6)
TS_p		10·0	8·6	8·6
LM		9·8	8·4	7·4
TS_s	18·5 (16·1)	17·3 (18·0)	17·3 (16·7)	18·2 (17·5)
TS_a	20·2 (17·7)	13·5 (14·7)	14·2 (14·7)	14·6 (15·7)

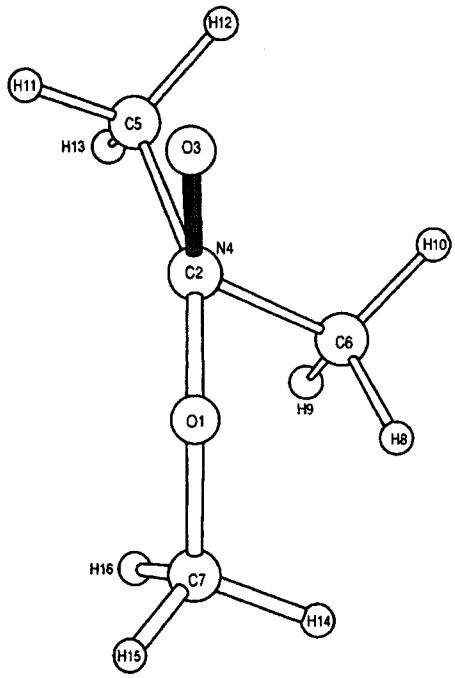


Figure 4. Optimized structure of **1** with the dihedral angle O3—C2—O1—C7 (α) fixed at 180°

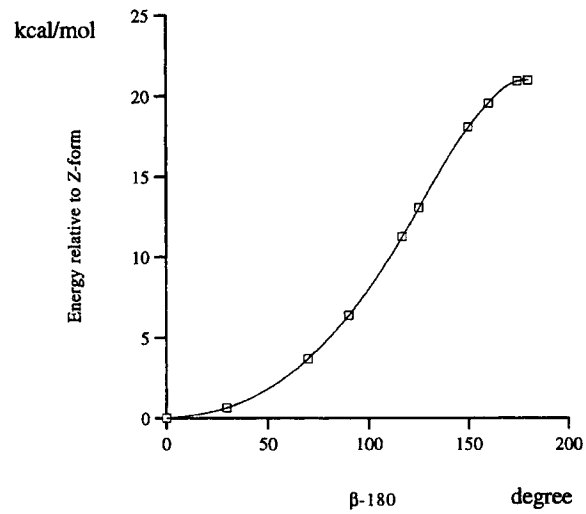


Figure 5. Energy profile for **1** with variation of dihedral angle C6—N4—O1—C7 (β)

than TS_a by 1·6 kcal mol^{-1}. Similar calculations on *N*,*N*-dimethylformamide (DMF) and *N*,*N*-dimethylacetamide (DMA) showed that the TS_a conformations are more stable than the others by 0·79 and 3·8 kcal mol^{-1}, respectively, which are in good agreement with the reported values of 0·23 (DMF) and 4·0 kcal mol^{-1} (DMA), calculated at the MP2/6–31 + G** level.[8] The bond angles of Y1—C2—N4 of TS_s for **2**–**4** are larger than those of corresponding TS_a by 3·5, 4·2, and 6·1°, respectively, but smaller by 1·4° in the case of **1**. This result may suggest that the unique properties of **1** arise from repulsion between the lone pair on O1 and that on N4 resulting in destabilization of its TS_a.

From the data in Table 2, rotational barriers about N4—C2 bonds, i.e. energy differences between the lower transition states and the ground states (*Z*-forms), are estimated to be 16·1, 14·7, 14·7, 15·7 kcal mol^{-1} for **1**, **2**, **3**, and **4**, respectively, indicating that chalcogen atoms have less effect on the barrier of rotation about N4—C2 bonds than about Y1—C2 bonds. For **1** and **2**, there have been several experimental studies on internal rotation about N4—C2 bonds, but the barrier varies widely depending on the solvents,[8] concentrations, and methods employed for measurements.[14j,m-o] For example, ΔH^* values of 15·5–22·9 (**1**) and 17·2–20·1 (**2**) kcal/mol^{-1},[14j,l] and ΔE^* values of 12·3–14·4 (**1**) and 13·0–14·5 (**2**) kcal mol^{-1},[14m-o] have been reported. Concerning theoretical calculations, there is one report which dealt with the rotational barrier of **1** but the transition state was not fully optimized.[14d] Hence it may be difficult to compare the present results directly with reported values.

Similar calculations on DMF and DMA at the MP2/3–21G(*)//HF/3–21G(*) level gave rotational barriers (TS_a) of 20·7 and 16·1 kcal mol^{-1}, respectively. These values are satisfactorily close to the reported barriers for DMF and DMA, i.e. 20·5 and 18·5 kcal mol^{-1} calculated at the MP2/6–31 + G**

Table 3. Selected structural parameters of TS_p, LM, TS_s and TS_a of **1**–**4**[a]

	Bond distances (Å)			Bond angle (°)				Dihedral angle (°)		
	C2—Y1	C2—N4	C2—O3	N4—C2—O3	O3—C2—Y1	Y1—C2—N4	C2—Y1—C7	O3—C2—N4—C5	C5—C2—N4—C6	O3—C2—Y1—C7(α)
Rotation about Y1—C2 bonds										
TS_p–**2**	1·817	1·356	1·215	123·2	119·5	117·4	96·9	−1·3	175·9	97·7
LM–**2**	1·799	1·362	1·214	123·2	118·4	118·4	102·6	−8·8	160·5	136·8
TS_p–**3**	1·972	1·356	1·214	123·4	118·8	117·7	94·1	−0·2	178·6	95·0
LM–**3**	1·965	1·358	1·213	123·4	118·9	117·7	96·5	−4·6	170·3	115·6
TS_p–**4**	2·213	1·356	1·216	123·0	116·8	120·2	92·5	0·2	−179·4	93·4
LM–**4**	2·194	1·355	1·216	123·5	114·9	121·6	100·7	−6·7	170·6	142·3
Rotation about N4—C2 bonds										
TS_s–**1**	1·359	1·407	1·199	127·1	121·9	111·0	118·0	114·4	131·2	0·0
TS_a–**1**	1·342	1·412	1·207	125·2	122·4	112·4	117·6	65·3	−130·5	0·0
TS_s–**2**	1·783	1·412	1·202	125·0	121·3	113·8	99·4	108·1	143·8	0·0
TS_a–**2**	1·750	1·427	1·205	125·2	124·5	110·3	99·5	65·6	−131·2	0·0
TS_s–**3**	1·944	1·414	1·199	124·8	121·8	113·4	97·1	109·6	140·8	0·0
TS_a–**3**	1·904	1·429	1·203	125·1	125·7	109·2	97·5	65·8	−131·5	0·0
TS_s–**4**	2·202	1·415	1·199	124·6	119·2	116·2	92·5	110·0	139·9	0·0
TS_a–**4**	2·146	1·434	1·202	124·8	125·1	110·1	93·6	65·3	−130·6	0·0

[a] All TS_s and TS_a structures have C_s symmetry

level[8] and ΔE^* values of 20·5[20] and 16·5[21] kcal mol^{-1} determined experimentally in the gas phase, respectively. These results indicate that our calculations afford sufficiently reliable rotational barriers.

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