Theoretical Study of the Mechanism of Dimerization of N,C-Disubstituted Carbodiimides

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Semiempirical calculations (AM1) have been carried out on the formation of 1,3-diazetidinediimines by dimerization of carbodiimides. The model cases of carbodiimide itself, HN=C=NH and N-amino-N'-methylcarbodiimide, $H_2N-N=C=N-CH_3$, have been studied. For the second compound, eight isomeric diazetidines can be obtained by cyclodimerization. The two most stable isomers are the bis(hydrazono)-1,3-dimethyldiazetidines of Z,Z and E,E configuration which correspond to the kind of structures actually formed. For the study of the kinetic aspects of the dimerization, the complete two-dimensional surface has been determined for carbodiimide itself. It appears that the asynchronous reaction is favoured over the synchronous approach. In the case of N-amino-N'-methylcarbodiimide, twelve asynchronous transition states have been calculated. The lowest transition state corresponds to the formation of 1-amino-3-methyl-2,4-bis(hydrazono)diazetidine, analogous to the diazetidine isomer whose existence has been postulated to explain the mass spectra of bis(heteroarylimino)-1,3-diaryldiazetidines.

Some time ago,[1] we described the reaction given in Scheme 1.
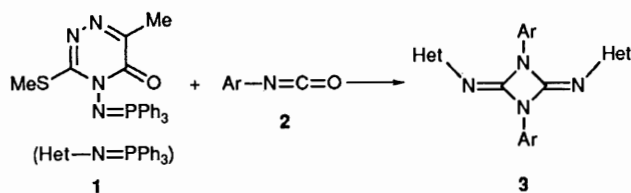
Scheme 1

When the heterocyclic iminophosphorane **1** reacted with a series of aryl isocyanates **2**, the only isolated product was a 1,3-diazetidinediimine **3** of Z,Z-configuration which exists as such both in the solid state (X-ray) and in solution (^{1}H and ^{13}C NMR spectroscopy). In a subsequent report,[2] we reported that besides the Z,Z-isomer, minor amounts of the E,E-isomer **4** were formed in some cases. Unfortunately, equilibration experiments failed since the 1,3-diazetidinediimines rearrange on heating.[1] Moreover, it has been proved that the Z,Z-isomer is indefinitely stable at room temperature.

4

Ar—N=C=N—Het

5

To explain the formation of **3** and **4** in the reaction between **1** and **2**, we postulated[1] that the reaction involves an initial aza-Wittig reaction between the phosphorane **1** and the isocyanate **2** to give a carbodiimide **5** which undergoes a $[\pi^2_s + \pi^2_a]$ cycloaddition to give the diazetidines **3** and **4**. In order further to understand this reaction, we decided to carry out a theoretical study of the transformation **5** $\longrightarrow$ **3** + **4**. To make the reaction computationally manageable, we adopted the

Table 1 Computed geometries for the carbodiimide H–N=C=N–H **7** by using different methods (mean values of distances in Å, and of angles in degrees)

Base	d(N=C)	d(H–N)	$\angle$(HNC)	$\angle$(NCN)
MINDO/3	1.227	1.015	125.9	157.6
MNDO	1.248	1.003	116.9	167.4
AM1	1.247	0.994	120.1	167.4
STO-3G	1.243	1.042	112.5	169.5
6-311^{++}G**	1.206	0.999	118.0	173.4 (ref. 4)
MP2/6-31G**	1.229	1.010	116.8	170.8 (ref. 4)

following simplifications: (a) the heterocyclic ring was replaced by an amino group and (b) the aryl substituent was replaced by a methyl group. With these modifications, the model carbodiimide **6** retains its N- and C-substituents. As for all asymmetric

$$H_2N-N=C=N-CH_3$$

6
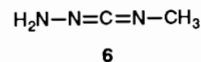
carbodiimides, eight 1,3-diazetidinediimines can be obtained by dimerization of **6** (Scheme 2). In the following discussion we will use a four-letter code to describe these compounds: substituents at position 1 and 3 of the diazetidine ring (C for methyl and N for amino) followed by the configuration of the exocyclic C=N bonds (first the =N–NH$_2$ bond and then the =N–CH$_3$ bond).

Results and Discussion

Relative Stabilities of the Different Isomers.—To begin with, we studied carbodimide itself, H–N=C=N–H **7**, as a model compound. Theoretical calculations using different methods (Table 1) show a small distortion for carbodiimide with regard to point group C_2. The N=C=N group is not exactly linear (the perfectly linear molecule is 2.2 kcal mol^{-1} higher in energy†), and the dihedral angle formed by H–N–N–H is not
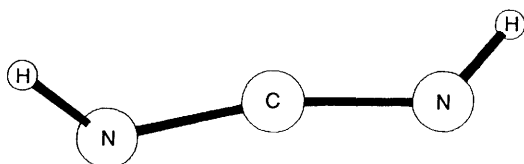
† 1 cal = 4.18 J
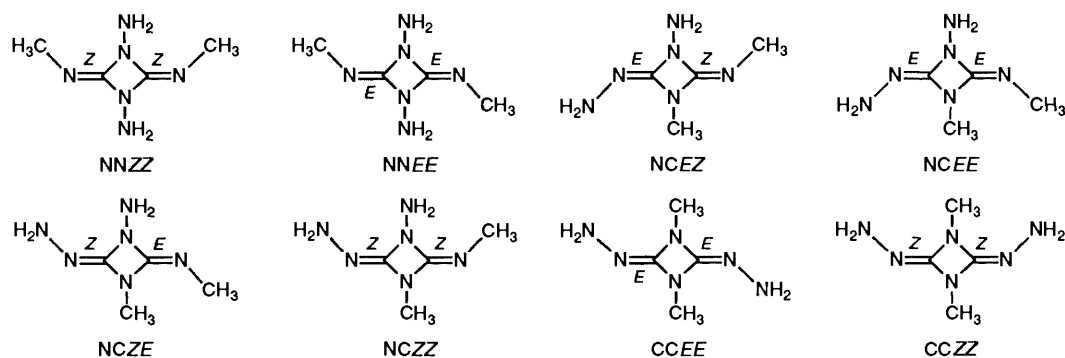
Scheme 2

Fig. 1   Geometry of the unsubstituted carbodiimide 7 (Table 1)

perfectly perpendicular. These findings are in good agreement with spectroscopic data[3] as well as with more precise calculations.[3–11]

As one can see in Table 1, semiempirical methods behave quite well as compared with *ab initio* methods with large basis sets and inclusion of correlation energy. Of the four methods of Table 1, AM1 at the closed-shell Hartree–Fock level was selected to carry out the complete study undertaken in this paper, since it combines the state-of-the-art semiempirical methods with their capability of being used for systems as large as those studied in this paper. It is obvious that, at present, studying the potential-energy surface of a substituted carbodiimide dimerization with *ab initio* methods (even using a minimal basis set) is beyond the capability of most theoretical groups. Chemical accuracy would require computing powers that will not be available for several years. With the AM1 method, a heat of formation of 41.4 kcal mol⁻¹ and the geometry shown in Fig. 1 were obtained.

Starting from carbodiimide 7, two diazetidines are possible (Scheme 2), the *cis* or HHZZ [Fig. 2(a)] and the *trans* or HHEE [Fig. 2(b)]. The corresponding heats of formation are 85.8 and 85.7 kcal mol⁻¹. The reaction energies with regard to the

separated reactants (two molecules of 7, 2×41.4 kcal mol⁻¹) are 3.0 for the *cis* and 2.9 kcal mol⁻¹ for the *trans* (the positive values correspond to endothermic reactions). The almost insignificant difference indicates that both isomers have the same probability of being formed. The examples described in the literature for diarylcarbodiimides, Ar–N=C=N–Ar, indicate that, indeed, these compounds cyclodimerize, but the resulting stereochemistry is now known.[12–15,*]

This thermodynamic approach to the dimerization of

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* We have carried out experiments corresponding to the dimerization of diphenylcarbodiimide and dibenzylcarbodiimide. The first yielded a 50:50 mixture of Z,Z and E,E isomers, characterized by the cyclic carbons at 143.85 and 143.30 ppm, respectively [²H₆]DMSO (Richter and Ulrich gave 144.2 and 144.6 ppm).[13] Some signals of the Z,Z isomer present a broadening due to hindered rotation of the central Z phenyl ring. Dibenzylcarbodiimide yields on dimerization a mixture of 80% of E,E diazetidine (cyclic carbon at 149.78 ppm, [²H₆]DMSO) and 20% of Z,Z isomer (cyclic carbon at 149.42 ppm). The number and intensities of the CH₂ signals (¹H and ¹³C) can be used to identify both isomers of bis(benzylimino)-1,3-dibenzyldiazetidine.[16]
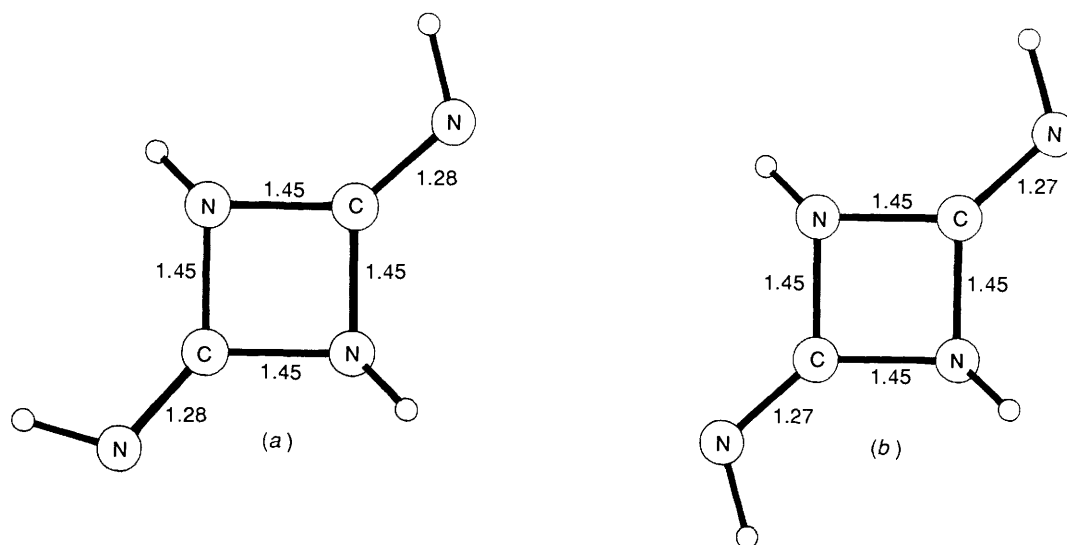

Scheme 3

Fig. 2   Geometries of: (a) *cis*-(HHZZ); and (b) *trans*-1,3-diazetidine (HHEE). Distances are given in Å.

Table 2 Computed geometries for the disubstituted carbodiimide R–N=C=N–R' **6** by using different methods (mean values of distances in Å, and of angles in degrees)

Base		d(N=C)	d(R–N)	$\angle$(RNC)	$\angle$(N=C=N)
MINDO/3	R = CH$_3$	1.18	1.37	175.2	157.4
	R' = NH$_2$	1.29	1.25	139.1	
MNDO	R = CH$_3$	1.24	1.45	127.6	165.1
	R' = NH$_2$	1.27	1.37	117.7	
AM1	R = CH$_3$	1.24	1.42	125.7	164.3
	R' = NH$_2$	1.27	1.35	122.9	
	R,R' = p-nitrophenyl[a]	1.24	1.40	132.0	169.7

[a] Experimental result, ref. 7.

Table 3 Heats of formation (energy of products less energy of the reactants) for the eight possible isomers of **6**

Isomer	ΔH/kcal mol^{-1}
NNZZ	7.0
NNEE	3.3
NCEZ	0.7
NCEE	3.0
NCZE	3.6
NCZZ	4.5
CCEE	−0.6
CCZZ	−1.3
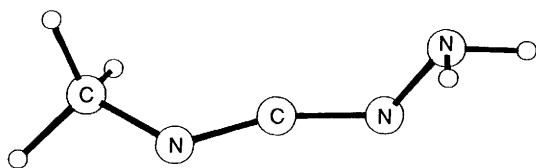
Fig. 3 Geometry of the N-amino-N'-methylcarbodiimide **6** (Table 2)

carbodiimides can be extended now to the amino(methyl)-substituted carbodiimide **6**. Its optimized geometry (Fig. 3 and Table 2) is very similar to that of carbodiimide **7**. The only interesting difference is that the N=C=N angle is more closed as a consequence of the presence of the CH$_3$ and NH$_2$ substituents. The heat of formation of **6** is 63.8 kcal mol^{-1}. Furthermore, the AM1 optimized geometries are quite close to experiment, thus confirming the reliability of our choice of level of calculation.

The eight dimers of Scheme 2 have been calculated. One can see that the ring C–N distances oscillate slightly between 1.45 and 1.48 Å. In general, the C=N, N–C and N–N bond lengths reflect the degree of double-bond character. In particular, the exocyclic C–N double bond length varies between 1.28 and 1.30 Å. These substituted 1,3-diazetidinediimines are non-planar compounds. One of the four corners of the ring is a few degrees out of plane, as in cyclobutane.[17a] The corresponding heats of formation are gathered in Table 3 and their respective geometries are depicted in Figs. 4(a)–(h).

The only compounds for which the reaction is exothermic are CCZZ (−1.3) and CCEE (−0.6 kcal mol^{-1}), $i.e.$, those corresponding to **3** and **4**. Thus, the calculations retrieve not only the two compounds actually isolated, but also their relative stability.

Kinetic Study.—The calculation of the potential barriers for the dimerization of carbodiimides was carried out within the framework of the theory of absolute rates, locating the transition states and determining their energies. To locate the transition states (TS) of carbodiimide dimerization, the reduced

potential-energy surface was determined using, as independent reaction co-ordinates, the distance between the atoms which become bonded in the diazetidine, since, as we will see later, they best describe the reaction. The orbital interaction of this reaction is similar to those of other cyclodimerizations, for instance, those of ketenes and allenes.[18] For the dimerizations of substituted carbodiimides, the search for TS was started at geometries whose reaction co-ordinates corresponded to those of the TS of non-substituted carbodiimide dimerization.

Therefore, as a first step, we calculated the dimerization of carbodiimide itself, $i.e.$ the reaction **7** ⟶ HHZZ + HHEE, since there are two possible isomers. The complete two-dimensional surface for the reaction leading to the HHEE isomer was calculated, using as variables each of the two lengths of the new bonds being formed (Fig. 5). An examination of the surface shows a potential height for the synchronous approach (diagonal of the square, about 66 kcal mol^{-1}); on the other hand, there is a valley for the asynchronous reaction, which corresponds to a non-simultaneous ring closure. No reaction intermediates were found.

Having established the non-synchronicity of the reaction, the approximate TS was located in the asynchronous region of the potential surface. The true TS was then found by minimizing the gradient norm (null gradient and only one imaginary vibrational frequency); its associated eigenvector indicated the motions of the atoms in the TS. The highly asymmetric transition structure (Fig. 6) presents distances of 1.49 and 2.16 Å for the 'partial' bonds, and of 1.34 and 1.36 Å for the original double bonds. Qualitatively, the reaction pathway corresponds to the shortening of the 'new' N–C distances and a small lengthening of the N–C double bonds of the carbodiimide to become the simple bonds of the diazetidine. The energy of the TS is 51.2 kcal mol^{-1} with respect to the reactants (two carbodiimides).

The most meaningful components of the transition vector represented in Fig. 6 show that the largest ones correspond to the C (0.63) and N (0.31) atoms which will bond to form the ring. Thus, the choice of the C–N distances as independent variables to compute the reduced potential surface of Fig. 5 was correct, since the reaction co-ordinate is composed essentially of these distances. Fig. 6 also shows that the reaction will proceed until the HHEE ($trans$) isomer is formed (remember that this is the major isomer obtained by dibenzylcarbodiimide dimerization).

For the dimerization of N-amino-N'-methylcarbodiimide **6**, the calculation of the bidimensional potential surface was unnecessary, since the eight asynchronous transitions states leading to the 1,3-diazetidinediimines of Scheme 1, were calculated and fully characterized starting from geometries similar to the one of Fig. 6. Emphasis must be given here to the fact that, while for the CC and NN isomers only one bond-breaking path is possible, for the NC isomers two bond-
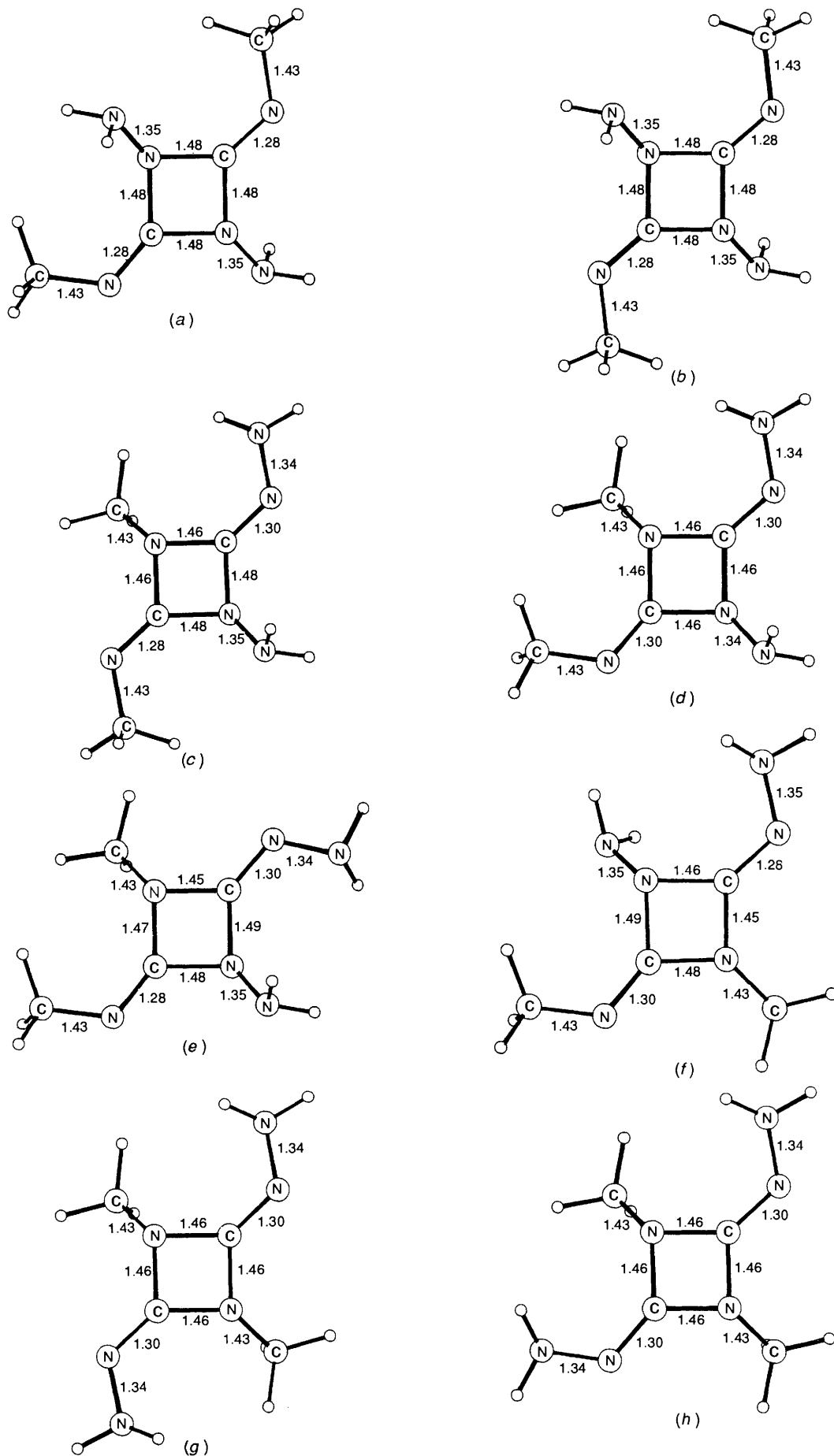
Fig. 4 Geometries (in Å) of the eight different isomers of N,N- and N,C-diazetidine: (a) NNZZ; (b) NNEE; (c) NCEZ; (d) NCEE; (e) NCZE; (f) NCZZ; (g) CCEE; and (h) CCZZ
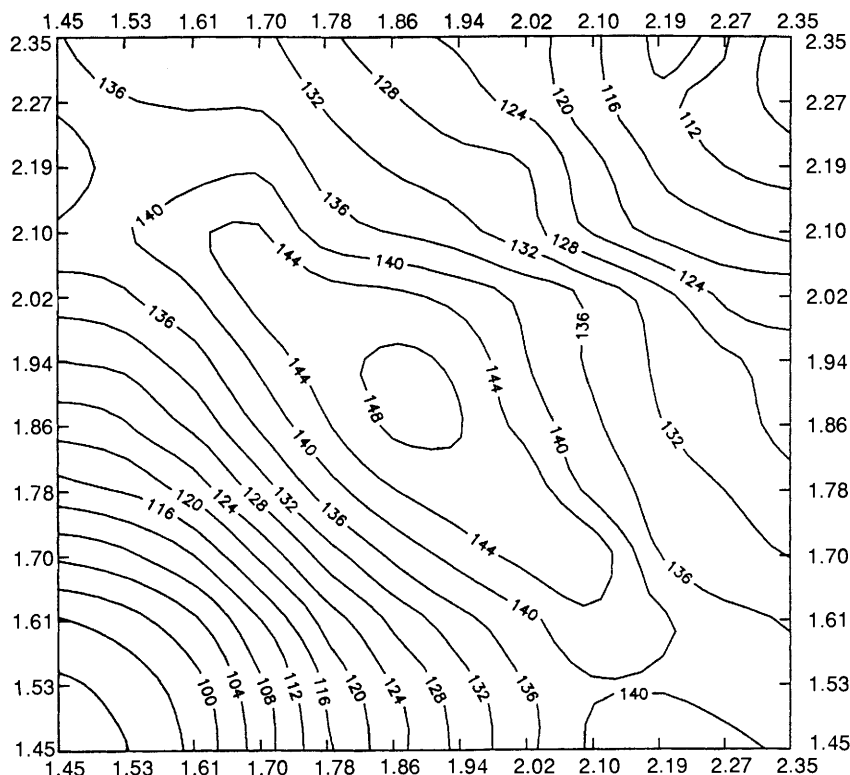
Fig. 5 Two-dimensional potential-energy surface corresponding to the dimerization of carbodiimide **7** to yield the HH*EE* isomer using the two forming C–N bonds as independent variables. Distances are given in Å, and energies (heats of formation) are given in kcal mol^{-1}
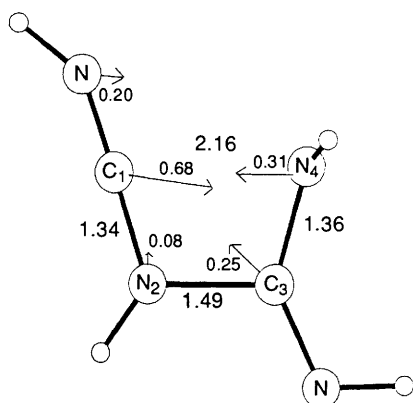

Fig. 6 Main geometrical parameters (in Å) and meaningful components of the transition vector of the transition state of carbodiimide cyclodimerization leading to the HH*EE* isomers

breaking paths are clearly possible. Thus, a total of 12 transition states have been located and characterized by having only an imaginary frequency corresponding to closure of the ring. Table 4 shows that the values of the four main distances do not differ very much among the twelve transition states. For the NC**C transition states, the C(1)–N(2) and N(4)–C(2) distances are slightly shorter and the C(3)–N(4) distances slightly longer. With respect to carbodiimide dimerization, the NN isomers are found later along the reaction co-ordinate N(4)–C(1) is shorter, whereas the NC*Z* isomers are found earlier. In all cases, the N(2)–C(3) bond is almost formed (final distance *ca.* 1.48 Å), whereas the C(1)–N(2) and C(3)–N(4) bonds still have double character (*ca.* 1.40 and 1.33 Å, respectively). The corresponding energy barriers are also represented in Table 4.

As can be seen, the lowest transition state corresponds to the NC*EZ*N isomer, that is, in the real case, to compound **8**. This compound has been neither isolated nor observed in the reaction. The compounds actually formed **3** (CC*ZZ*) and **4**
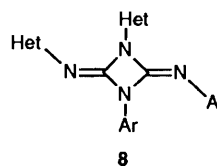
(CC*EE*) have the highest barriers. No isomers other than the CC ones were observed, although when the mass spectra of compounds **3** were recorded, two kinds of fragment were found:[1] [Het–N=C=N–Ar]$^{\cdot+}$ corresponding to the expected cycloreversion and [Ar–N=C=N–Ar]$^{\cdot+}$. To explain the origin of this second fragment, it was necessary to assume that, under mass spectrometry conditions, diazetidine **3** is in equilibrium with diazetidine **8** (Scheme 4).
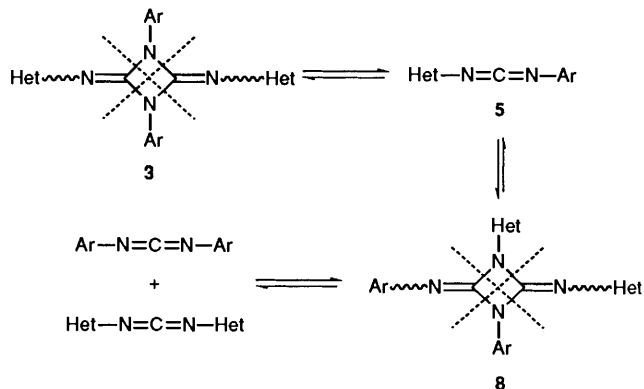
Scheme 4

In conclusion, even with the simplifications which have been introduced, theoretical calculations provide a consistent picture of the mechanism of cyclodimerization/cycloreversion of carbodiimides.

Table 4 Geometries (Å) of the transition states and energy barriers (kcal mol^{-1}) corresponding to the dimerization of carbodiimides. For NC isomers, a terminal N means that breaking is made in such a way that amino groups come into closer proximity and methyl groups separate. A terminal C indicates the opposing situation.

Starting material	C(1)–N(2)	N(2)–C(3)	C(3)–N(4)	N(4)–C(1)	Final product	Energy barrier[a]/kcal mol^{-1}
7	1.36	1.49	1.34	2.16	HH*EE*	51.2
6	1.37	1.48	1.33	2.11	NN*ZZ*	53.7
	1.36	1.48	1.33	2.17	NN*EE*	57.9
	1.40	1.48	1.32	2.24	NC*EZ*N	53.5
	1.38	1.53	1.36	2.16	NC*EZ*C	47.7
	1.40	1.48	1.32	2.22	NC*EE*N	51.9
	1.37	1.51	1.37	2.19	NC*EE*C	52.5
	1.40	1.52	1.32	2.25	NC*ZE*N	53.2
	1.38	1.50	1.37	2.21	NC*ZE*C	53.0
	1.40	1.48	1.32	2.27	NC*ZZ*N	55.4
	1.39	1.51	1.37	2.13	NC*ZZ*C	47.9
	1.40	1.51	1.34	2.24	CC*EE*	59.9
	1.40	1.54	1.34	2.24	CC*ZZ*	59.8

[a] Difference between the energies of the transition state and reactants.

(*a*) The transition state which lies in the progression from reactants to products has a clear asymmetric structure.

(*b*) If it is assumed that the reaction is under thermodynamic control, then the results of the calculations explain the formation of **3** and (in a minor amount) of **4**.

(*c*) Kinetic control is not observed under laboratory conditions: products **8** corresponding to the lower-energy pathway only appear in the mass spectrometer.

Computational Details.—The semiempirical MNDO,[19] MINDO/3,[20] AM1,[21] and the *ab initio* SCF STO-3G[17b] methods were used in their original formalism. The AMPAC[22] program was used for semiempirical optimizations, whereas the GAUSSIAN 86[23] program was used for *ab initio* calculations.

Acknowledgements

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