simple atomic and bond labels that reflect their physical nature and in some (additive) manner their topology. Our recent results[5,14] and the results presented in this paper support the assumption that these descriptors are useful for a proper representation of functional groups for purposes of neural network applications.

The descriptors are constructed directly from the structural formulas of functional groups in a way immediately reflecting their structural features. We believe that this is the main superiority of the used descriptors with respect to other potentially applicable descriptors for chemical-reactivity studies (e.g., Ugi's[22] BE matrix used by Elrod[4a,b] or ad hoc chosen physico-chemical parameters used by Luce[4c]). Moreover, for those special cases dealing with specific chemical-reactivity effects (e.g., regioselectivity or site selectivity), the structural descriptors used may be directly enlarged by additional parameters. Those parameters could correspond to the properties of reactants or functional groups determined by the whole structure (e.g., inductive and resonance σ constants, steric hindrance parameters, charges of σ or π skeleton,[20] a kind of topological index, etc.).

Inductive and resonance σ constants represent a very important approach to describe properties of functional groups, in particular their influence to synthons[7,8] undertaking chemical reactions. We have demonstrated that these parameters are useful for classification by feed-forward neural networks. The descriptors are also adequate in the classification of the influence of functional groups to reaction cores. The adapted neural network was tested for its ability to predict inductive and resonance σ constants for 21 functional groups, which form the testing set (see second part

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of Table II). In most cases, the sign of the predicted σ constants is retained, and for the functional groups $-N(Ph)_2$, $-NHCN$, and $-CH_2Ph$, one constant has the opposite sign. Two of these groups contain phenyl, and therefore, their precise description should likely involve additional descriptors that reflect more adequately their anomalous physical properties.

Activities of hidden neurons correspond[2] to an internal representation of functional groups. These activities were used for simple cluster analysis of functional groups. That is, the whole training set is divided in disjoint subsets, where these clusters are composed of functional groups with similar hidden-activity vectors. For these purposes, the training set was composed of all 87 functional groups (see Table II), and the neural network was again subjected to the adaptation process. After 5000 iterations, the value of the objective function yielded $E = 0.2$ and $|\text{grad } E| = 10^{-4}$. The hidden activities of all 87 functional groups were used as an input for cluster analysis; the obtained results for 5 and 10 clusters are presented in Tables IV and V. The obtained clustering of functional groups is chemically plausible as they have similar structural features and similar inductive and resonance properties. Moreover, the present results are closely related to the cluster analysis of functional groups carried out by Hansch and Leo[21] based on different properties that characterize the functional groups (lipophilicity, molecular refractivity, inductive and resonance σ constants, and binary H-bonding).

In conclusion, it seems that the neural network approach gives both a useful and simple mathematical model for the classification and prediction of molecular properties manifested by organic chemical reactivity. This approach allows the construction of formal methods that solve in some binary manner the difficult problem of chemical reactivity for purposes of computer-aided organic synthesis design.

The Equilibrium Conformation of Ethyl Isocyanate Revisited

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Abstract: The equilibrium conformation of ethyl isocyanate was reinvestigated by molecular orbital calculations using second-order Møller–Plessett perturbation theory and a 6-31G** basis set. It was shown that the inclusion of electron correlation is of crucial importance in the prediction of the equilibrium structure for this molecule. According to the calculations, there are two stable conformers, the gauche and the trans, of which the gauche has lower energy. The cis form does not correspond to a local energy minimum. A new interpretation for the experimental microwave spectra is suggested. The known infrared spectrum was also assigned using frequency calculations.

Introduction

The geometric structure of pseudohalides is still subject to uncertainty in those cases where experimental information on the geometry is not available. This is caused by the fact that ab initio calculations seem to have difficulties in predicting the correct geometry of these molecules.[1-3] The most probable reason for this effect is that the potential energy curve of pseudohalides is rather shallow around the minimum.[1,2] In order to circumvent this problem, it is often necessary to use higher than usual accuracy in the gradient calculation.

For all pseudohalides investigated so far, it was necessary to include polarization functions and correlation energy also had to

be incorporated into the calculations to obtain geometries similar to the experimental ones. On using Gaussian basis sets of quality 3-21G or better in an SCF calculation but without polarization functions and including the effects of correlation, always a linear C–N–C and N–C–O angle was obtained for methyl and tertiary-butyl isocyanates.[1,2] In a publication by Sullivan, Durig, Durig, and Cradock,[4] however, ab initio calculations predicted these angles to be less than 180° in ethyl isocyanate using a 3-21G basis

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The Equilibrium Conformation of Ethyl Isocyanate

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Table I. Calculated Equilibrium Geometry of $CH_3CH_2NCO^a$

	cis[b]	trans	gauche
energy	−246.611325	−246.611116	−246.611655
$r(H—C_1)$	1.088	1.088	1.088
$r(H—C_1)$	1.087	1.087	1.087
$r(C—C)$	1.519	1.516	1.519
$r(C_2—H)$	1.089	1.090	1.090
$r(C—N)$	1.444	1.448	1.447
$r(N=C)$	1.214	1.216	1.214
$r(C=O)$	1.191	1.190	1.191
$\angle NCO$	172.56	172.40	172.23
$\angle CNC$	138.33	137.32	136.51
$\angle CCN$	113.07	109.90	112.10
$\angle HC_2C_1$	110.59	110.37	110.40
$\angle HC_2H$	107.07	107.71	107.25
$\angle HC_1C_2$	110.47	110.11	110.55
$\angle HC_1H$	108.51	108.50	108.51
μ_t	3.084	2.947	3.367

[a] Calculated using a 6-31G** basis set at the MP2 level; bond lengths in Å, bond angles in degrees, energy in au, and dipole moment in D. [b] This structure is a first-order saddle point. See text for details.

set. This contradiction was the original basis for this work. On carrying out calculations using a 3-21G basis, it was found that the geometry given in Table III of ref 4 does not correspond to a minimum and the molecule should indeed have a linear C–N–C–O chain at this level of theory, if the largest accepted value of the gradient is chosen to be at least as small as 5×10^{-5}. With less stringent convergence criteria, the final gradient depends on the starting point of the optimization. All other structural parameters in Table III of ref 4 with every other basis set could be reproduced in this work. However, having performed frequency calculations using the same basis as in the optimizations, it was soon found that the cis structure (NCO eclipsing the methyl group) in all cases corresponds to a transition state.

The experimental studies on ethyl isocyanate also contradict the calculations in ref 4. The microwave spectrum of ethyl isocyanate[7,8] consists of a large number of absorption lines, some of which were assigned to the cis conformer. It was also shown in ref 7 that lines due to another conformer are also present, although this conformer was not identified. The electron diffraction data on ethyl isocyanate[9] were found to be more consistent with a conformer between the cis and the gauche structure, nearer to the gauche. However, on the basis of the microwave results, it was interpreted in terms of a single cis form. Because of the obvious contradictions between the experimentally determined structure and previous ab initio structures, which favored a trans minimum-energy geometry, it was decided to optimize the geometry of the gauche conformer as well as the cis and the trans. It was hoped that this would resolve the above controversy and that the theoretical equilibrium conformation of this molecule could be predicted.

Calculations

All the calculations in this work were carried out using the CADPAC quantum chemistry package.[5] The geometry of the molecule was first optimized using the gradient method.[6] The largest accepted value of the gradient was 5×10^{-5}. The predicted displacements at equilibrium were checked, and these were always below 10^{-4} Å. The vibrational frequencies were then calculated at the minimum-energy geometry, using analytic second derivatives. A standard 6-31G** basis set was used in the calculations. Furthermore, the optimum geometry and the vibrational frequencies were also calculated, allowing partially for the effects of correlation using second-order perturbation theory.

Results and Discussion

The results of the geometry optimizations are shown in Table I. The geometries of the cis, gauche, and trans conformers were optimized separately. It was found that the cis conformer lies

Table II. Calculated[a] and Experimental[b] Vibrational Frequencies of $CH_3CH_2NCO^c$

| fundamental	experimental	gauche	trans
CH_3 antisym stretch	2991	3238	3244
CH_3 sym stretch	2942	3138	3145
CH_2 sym stretch	2906	3145	3131
NCO antisym stretch	2285	2397	2404
CH_2 def	1480	1576	1556
CH_3 antisym def	1473	1561	1570
CH_3 sym def	1437	1467	1470
NCO sym stretch	1393	1484	1481
CH_2 wag	1352	1426	1420
CH_3 rock	1140	1200	1187
C—C stretch	1098	1143	1153
C—N stretch	807	840	832
N=C=O bend	640	627	621
CCN bend	425	427	393
CNC bend	144	148	135
CH_3 antisym stretch	2996	3250	3256
CH_2 antisym stretch	2956	3209	3188
CH_3 antisym def	1458	1552	1552
CH_2 twist	1258	1345	1348
CH_3 rock	981	1031	1060
CH_2 rock	788	825	822
N=C=O bend	610	573	571
CH_3 torsion	265	298	281
C—N torsion	68	49	29

[a] An MP2/6-31G** calculated structure; see text for details. [b] From ref 4. [c] In cm⁻¹.

Table III. Calculated[a] and Experimental[b] Rotational Constants of $CH_3CH_2NCO^c$

	A	B	C
experimental	14110.25 ± 3	3067.01 ± 0.02	2605.01 ± 0.02
cis	14316	3008	2560
gauche	15867	2807	2498
trans	36018	2560	2164

[a] Obtained at the optimized MP2/6-31G** geometry. [b] From ref 4. [c] In MHz.
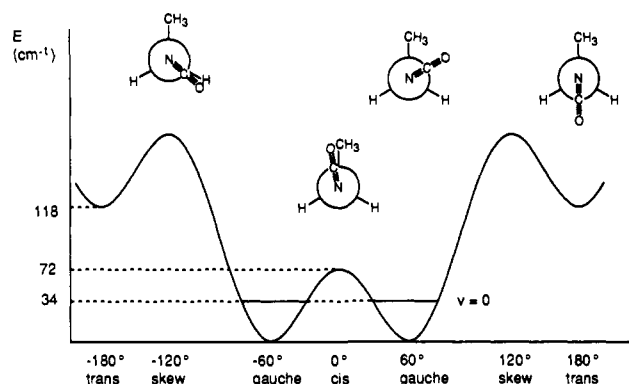
Figure 1. Relative energies of the different conformers of CH_3CH_2NCO.

slightly lower in energy than the trans form and the gauche form has the lowest energy. In order to check whether the optimized geometries really represent a minimum on the potential energy surface, the vibrational frequencies of ethyl isocyanate were also calculated. The calculated frequencies were all positive for the trans and gauche forms. These are all assigned and given in Table II together with the experimental frequencies from ref 4. The frequency calculations on the cis conformer, however, gave one negative frequency (-62 cm⁻¹), indicating that the cis form does not correspond to a minimum-energy structure. These results can be rationalized using an energy diagram, given in Figure 1. In this Figure, the $v = 0$ level has been marked, on the basis of the zero-point energy, obtained from the experimental infrared spectrum, of 34 cm⁻¹.[4] It is therefore expected that a large-amplitude hindered torsional motion will exist around the minimum, which may only become free at higher levels of excitation of this vibration.

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(6) Pulay, P. *Mol. Phys.* **1969**, *17*, 197.

In an earlier microwave study on ethyl isocyanate,[7] the cis conformer was predicted to be the most stable. This conclusion was reached by calculating the moments of inertia at some trial geometries for the four possible conformers and finding that the best agreement was achieved at the cis form. The rotational constants from MW spectroscopy are given in Table III together with the ones derived in this work from the minimum-energy structure in the cis, trans, and gauche forms. As can be seen, all calculated constants are outside the error bounds of the experimental values. Additionally, the calculated gauche constants cannot be compared directly with the experimental values, due to the large-amplitude torsional motion. In this case, the moments of inertia have to be determined as an average value around the minimum structure and this average has to be weighted according to the value of the wave function. Since the vibrational wave function will have larger amplitude on the cis side than on the skew side due to the smaller barrier height, the moments of inertia and thus the A, B, and C constants for the gauche conformer will have values nearer to the cis value. To summarize, the accuracy of the ab initio geometry, or that of any predicted structure, does not allow the choice between the cis and gauche form to be made merely on the basis of best agreement of rotational constants. However, further conclusions on the possible observation of different conformers can still be made on the basis of the energy level diagram in Figure 1.

According to Figure 1, there are three cases depending on the level of excitation of the torsional vibration, if the coupling of this vibration with the C–N–C bend is neglected. At the $v = 0$ vibrational level, only the gauche conformer is expected to be present. Due to the double minimum at $\pm 57.8°$, splitting of the vibrational level will take place, caused by tunneling through the barrier. Above the $v = 1$ or 2 level, depending on the exact value of the torsional vibrational frequency, the energy is clearly over the cis barrier. These levels are readily populated at room temperature, and when this is the case, the torsional motion will be unhindered between the two skew energy barriers, with the average conformation being cis. At even higher vibrational levels, the torsional motion becomes completely free. As the frequency of the overall rotation is very different from that of the torsional vibration, it can be assumed that they will not couple and, as a result, the internally rotating groups can be considered as two coaxial flywheels connected by a semirigid axis, as was done, for example, in the analysis of the infrared torsional spectrum of ethane.[10] The situation is slightly different if coupling between the C–N–C bend and the torsional vibration is taken into account. These have the experimental vibrational frequencies of 68 and 144 cm^{-1}, respectively.[4] Tunneling through the barrier would not occur in this case, as the two minima are connected via the bending motion. It must be noted that, in any case, some further splitting of the vibrational energy levels is expected, due to the other (trans) minimum, which lies much higher in energy.

The above conclusions thus have to be compared with the results of the experimental microwave spectrum. In ref 7, the cis conformer was seen together with some other unidentified conformers. It was proved that the other conformer cannot be trans or skew, but the presence of the gauche form was not studied. As a result,

if the coupling between the C–N–C bend and the torsional motion can be neglected, the cis levels, identified as $v = 0, 1, 2, ...,$ are in reality the $v = 1, 2, 3, ...$ vibrational states of the torsional motion and the $v = 0$ level will correspond to a configuration between the cis and the gauche form, nearer to the gauche, as discussed above. The transitions originating from this level will in that case show some complicated splitting pattern, which may indeed be due to the unidentified rotamer in ref 7. The strong anharmonicity of the satellite pattern in ref 7 gives a possible indication that a barrier at the cis configuration must exist. Thus, the results of the microwave investigation are in good agreement with the calculated results in this work, but there is clearly a need for a reinvestigation of the experimental microwave spectra in view of the present findings.

The results of electron diffraction studies[9] are also in good agreement with the results of this present study. The experimental electron diffraction data best fitted a conformation between the cis and the gauche, closer to the gauche structure. As in the discussion above for the moments of inertia, exactly such a structure would be expected when the large-amplitude torsional motion is taken into account. The choice of the cis conformer in ref 9 was made on the basis of the MW studies,[7] although the cis configuration did not so well fit the experimental data. It must be noted, however, that the structure, determined by electron diffraction, is expected to be an average over different vibrational levels of the molecule and therefore far-reaching conclusions cannot be drawn on the basis of this method alone.

The only previous theoretical study on the cis and trans conformers of this molecule was performed by Sullivan et al.,[4] who found the trans conformer to be the minimum-energy structure. Calculations carried out in this work with the same basis sets (STO-3G, 3-21G, 6-31G*) and without the effects of electron correlation also confirmed that the trans form is the minimum-energy structure. However, when electron correlation is allowed for by the MP2 method, the cis conformer will be considerably lower in energy than the trans and the gauche will have the minimum energy. This latter conformer was not at all studied in ref 4. The cis conformer was found to be a transition state in this work with all basis sets, with and without the effects of correlation, although this fact was not recognized in ref 4.

Conclusions

In this work, the gauche structure was found to be the minimum-energy structure of ethyl isocyanate. It was proved that the accuracy of the ab initio geometry, or that of any predicted structure, did not allow the choice between the cis and gauche form to be made merely on the basis of best agreement of rotational constants. The choice was based on the fact that the potential energy curve at the MP2/6-31G** level of theory has a local minimum at the gauche form, whereas the cis form is a transition structure. Contrary to previous theoretical work, which did not include the effects of correlation, it is unambiguously indicated by the calculations in this work that although the trans structure is stable, it cannot be populated at the $v = 0$ vibrational level. This result is supported by both the microwave and the electron diffraction data. The calculations also provide some possible explanation as to the complicated nature of the microwave spectra. It would therefore be of great interest to reanalyze the experimental microwave spectra, including the effects of the large-amplitude torsional vibrations, and thus unambiguously establish the experimental conformation of ethyl isocyanate.

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