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The Anomeric Effect in (Fluoromethyl)dimethylamine, $CH_2FN(CH_3)_2$

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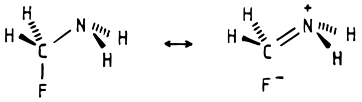
Abstract: The molecular structure of (fluoromethyl)dimethylamine, $CH_2FN(CH_3)_2$, has been determined by gas electron diffraction (GED), ab initio (HF/3-21G$^{(*)}$ (polarization functions only at nitrogen), and MP2/6-311G(2d,p)), and local density functional (VWN/TZVP) calculations. According to the GED analysis only the anti conformer (C−F bond antiperiplanar to the nitrogen lone pair) is present. The following skeletal geometric parameters (r_a distances and $\angle_\alpha$ angles with 3σ error limits) were obtained: N−CH$_2$F = 1.408(13) Å, N−CH$_3$ = 1.466(9) Å, C−F = 1.410(5) Å, (C−N−C)$_{\text{mean}}$ = 111.6(10)°, and N−C−F = 115.9(24)°. The results are discussed on the basis of the generalized anomeric effect. The theoretical calculations predict a second stable conformer with synclinal orientation of the C−F bond and 4.5−5.3 kcal mol^{-1} higher in energy.

Introduction

The anomeric effect has originally been formulated to rationalize structures, conformational properties, and reactivities of cyclic, oxygen-containing carbohydrates, especially of sugars.[1] The same stereoelectronic interactions, however, operate equally effectively on the conformation of acyclic compounds which contain atoms with lone pairs, such as O, N, and F. These interactions have been termed the generalized anomeric effect.[2] Fluoromethylamine, CH_2FNH_2, became the most prominant model compound for theoretical studies of this effect,[3−9] because N possesses only a single lone pair orbital, which is higher in energy than those of O or F, and because the σ^* orbital of the C−F bond is low in energy. Thus, the HOMO-LUMO energy separation is small and one of the strongest anomeric effects is predicted for this molecule. The interaction between the nitrogen lone pair and the antibonding C−F orbital (lp(N) → σ^*(C−F)) results in stabilization of the antiperiplanar orientation of the C−F bond relative to the nitrogen lone pair. Ab initio calculations at various computational levels give conflicting results about the stability of a second conformer with synperiplanar orientation of the C−F bond. The classical interpretation of this lp(N) → σ^*(C−F) interaction, which involves a double-bond−no-bond resonance structure, reveals the structural consequences of the anomeric effect. Besides the stabilization of the anti conformer, shortening of the N−C bond, lengthening of the C−F bond, and increase of the N−C−F angle and the angles around nitrogen are expected.

Scheme 1



To our knowledge, the synthesis of CH_2FNH_2 has never been reported in the literature and this compound is not expected to possess sufficient stability for a structural analysis. On the other hand, the methyl-substituted derivative $CH_2FN(CH_3)_2$ has been known for ca. 25 years and is a stable compound at room temperature.[10] Thus, this compound is highly suited for an experimental study of the structural consequences of the anomeric effect. As a matter of fact, the lp(N) → σ^*(C−F) interaction is expected to be even stronger in $CH_2FN(CH_3)_2$ than in CH_2FNH_2 since the electron donating methyl groups raise the lp(N) energy and thus lower the HOMO-LUMO energy difference. The anomeric effect is also reflected in the reactivity of this amine. With strong electrophiles it reacts as a source of fluoride ions, which can be explained by the following equilibrium: [11]

$$FCH_2(CH_3)_2 \leftrightarrow F^-CH_2{=}N^+(CH_3)_2$$

The ^{19}F-NMR spectrum gives further evidence of such an equilibrium since a single signal is observed at room temperature and the expected triplet occurs at lower temperatures.[10,11] We report here the result of a structure analysis using gas electron diffraction (GED). Unfortunately, we were not yet able to assign the complex microwave spectrum and derive rotational constants. A joint analysis of GED intensities and rotational constants would have reduced the experimental error limits for geometric parameters considerably. Vibrational amplitudes, which were derived from an approximate valence force field, were used in the GED analysis. The experimental investigation

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(1) (a) Kirby, A. J. *The Anomeric Effect and Related Stereochemical Effects at Oxygen*; Springer: Berlin, 1983. Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry;* Pergamon: Oxford, 1983; and references therein.

(2) Lemieux, R. U. *Pure Appl. Chem.* **1971**, *25*, 527.

(3) Schleyer, P. v. R.; Kos, A. J. *Tetrahedron* **1983**, *39*, 1141.

(4) Pinto, B. M.; Schlegel, H. B.; Wolfe, S. *Can. J. Chem.* **1987**, *65*, 1658.

(5) Schleyer, P. v. R.; Jemmis, E. D.; Spitznagel, G. W. *J. Am. Chem. Soc.* **1984**, *107*, 6393.

(6) Reed, E. A.; Schleyer, P. v. R. *Inorg. Chem.* **1988**, *27*, 3969.

(7) Radom, L.; Hehre, W. J.; Pople, J. A. *J. Am. Chem. Soc.* **1972**, *94*, 2371.

(8) Irwin, J. J.; Ha, T. K.; Dunitz, J. D. *Helv. Chim. Acta* **1990**, *73*, 1805.

(9) Rastelli, A.; Cocchi, M. *J. Chem. Soc., Faraday Trans.* **1991**, *87*, 249.

(10) Böhme, H.; Hilp, M. *Chem. Ber.* **1970**, *103*, 104.

(11) Knunyants, L.; Delyagina, N. I.; Igumnov, S. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1981**, 857.

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Table 1. Geometric Parameters for $CH_2FN(CH_3)_2$ from GED and Theoretical Calculations

	GED^a	HF/3-21G$^{(*)}$	MP2/6-311G(2d,p)	VWN/TZVP^b
$(N-C)_{mean}$	1.446(6) p_1	1.448	1.438	1.423
$\Delta NC=(N-C2)-(N-C1)$	0.058(17) p_2	0.050	0.050	0.054
N−C1	1.408(13)	1.415	1.405	1.387
N−C2	1.466(9)	1.465	1.455	1.441
C−F	1.410(5) p_3	1.418	1.413	1.431
$(C-H)_{mean}$	1.112(3) p_4	1.083	1.092	1.105
$(C-N-C)_{mean}$	111.6(10) p_5	111.9	112.8	113.8
$\Delta CNC=(C1NC2)-(C2NC2')$	1.5[5]^c	0.8	1.5	2.0
C1−N−C2	112.1(11)	112.0	113.3	115.1
C2−N−2′	110.6(12)	111.2	111.8	113.1
N−C−F	115.9(24) p_6	112.7	113.3	113.3
$(H-C-H)_{mean}$	109.4(10) p_7	109.0	109.1	108.7
tilt $(CH_3)^d$	2.2^e	2.1	2.2	1.9
$\phi(C2'-N-C2-H)$	178.9^e	177.9	178.9	176.9

^{a} r_a distances in Å and $\angle_\alpha$ angles in deg; error limits are 3σ values. For atom numbering see Figure 3. ^{b} Local density functional approximation[14] with polarized triple-ζ basis set. ^{c} Not refined, estimated uncertainty in square brackets. ^{d} Tilt of CH_3 group toward nitrogen lone pair. ^{e} Not refined.

is supplemented by theoretical calculations applying ab intio and local density functional methods.

Theoretical Calculations

The main interest in these calculations was the study of the conformational properties of $CH_2FN(CH_3)_2$. The potential function for internal rotation around the $N-CH_2F$ bond was calculated by optimizing the geometry at various fixed torsional angles ϕ(lpNCF) with the HF/3-21G$^{(*)}$ method. G$^{(*)}$ implies polarization functions on nitrogen only. Previous calculations for $CF_3N(CH_3)_2$ and $(CF_3)_2NCH_3$[12] and for other amines with fluorinated alkyl groups (see e.g. ref 13) demonstrated that this method reproduces experimental N−C bond lengths and C−N−C angles very well. The resulting potential curve (Figure 1) possesses minima at ϕ(lpNCF) = 180° and 56° ($\Delta E = 4.5$ kcal mol^{-1}). The syn structure (ϕ(lpNCF) = 0°) is predicted to be a transition state with respect to internal rotation and stable with respect to inversion at nitrogen. A similar potential curve with minima at 180° and 43° ($\Delta E = 5.2$ kcal mol^{-1}) is obtained with the local density functional (LDF) approximation of Vosko, Wilk, and Nusair[14] using a polarized triple-ζ basis set (VWN/TZVP, program DGAUSS[15]). This method predicts that the syn structure is unstable with respect to inversion at nitrogen. A high-level (MP2/6-311G(2d,p)) ab initio structure optimization was performed for the anti conformer, to obtain a reliable value for the difference between the C−N−C angles. Because of high correlations, this difference could not be refined in the GED analysis (see below). All ab initio calculations were performed with the GAUSSIAN 92 program system.[16] The theoretical geometric parameters for the anti conformer are compared with the experimental values in Table 1.

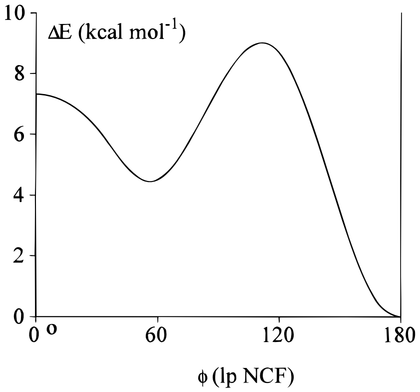

Figure 1. Calculated (HF/3-21G$^{(*)}$) potential curve for internal rotation around the $N-CH_2F$ bond.

GED Analysis

The radial distribution function (RDF) was calculated by Fourier transform of the molecular scattering intensities which were multiplied with an artificial damping function $\exp(-\gamma s^2)$ ($\gamma = 0.0019$ Å^2). The peak at ca. 2.9 Å in the experimental RDF (Figure 2), which correponds to the nonbonded C···F distances, is reproduced only with a molecular model which has the C−F bond anti to the lp(N). Preliminary geometric parameters which were derived from the RDF were refined by least-squares fitting of the molecular intensities. The intensities were multiplied with a diagonal weight matrix and known scattering amplitudes were used.[17] The two N−C and the C−F bond lengths and the one-angle nonbonded distances C···C and N···F are closely spaced which results in large correlations between these bond lengths, between the skeletal bond angles, and between these parameters and the respective vibrational amplitudes. In the least-squares refinement a mean N−C bond length $(N-C)_{mean} = {}^1/_3\,[(N-C1) + 2(N-C2)]$, the difference $\Delta NC = (N-C2) - (N-C1)$, a mean CNC angle $(CNC)_{mean} =$

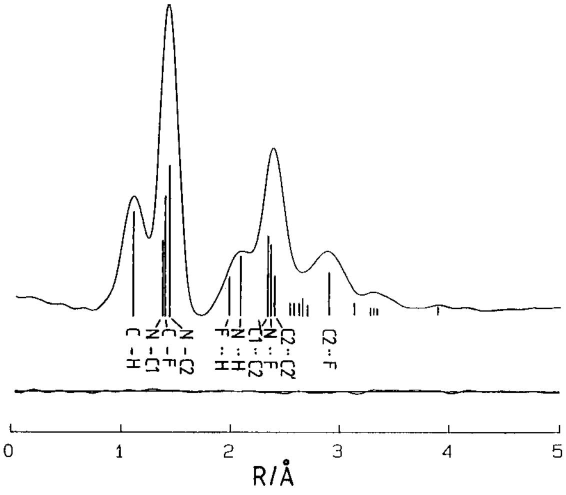

Figure 2. Experimental radial distribution function and difference curve. The positions of important interatomic distances are indicated by vertical bars. For atom numbering see Figure 3.

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(12) Jin, A.; Zhu, X. L.; Kirchmeier, R. L.; Shreeve, J. M.; Patel, N. R.; Oberhammer, H. *J. Mol. Struct.* **1994**, *323*, 129.

(13) Dimitrov, A.; Mack, H. G.; Rüdiger, S.; Seppelt, K.; Oberhammer, H. *J. Phys. Chem.* **1994**, *98*, 11401.

(14) Vosko, S. H.; Wilk, L.; Nusair, M. *Can. J. Chem.* **1980**, *58*, 1200.

(15) Andzelm, J. W.; Wimmer, E. *J. Chem. Phys.* **1992**, *96*, 1280.

(16) GAUSSIAN 92 / DFT, Revision G.2, M. J. Frisch, G. W. Trucks, H. B. Schlegel, M. W. Gill, B. G. Johnson, M. W. Wong, J. B. Foresman, M. A. Robb, M. Head-Gordon, E. S. Replogle, R. Gomperts, J. L. Andres, K. Raghavachari, J. S. Binkley, C. Gonzales, R. L. Martin, D. J. Fox, D. J. Defrees, J. Baker, J. J. P. Stewart, J. A. Pople, Gaussian Inc. Pittsburgh, PA, 1993.

(17) Haase, J. *Z. Naturforsch.* **1970**, *25a*, 936.

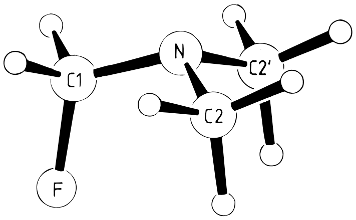

Figure 3. Molecular Model for the anti conformer with atom numbering.

Table 2. Interatomic Distances and Vibrational Ampitudes l_k from GED and Calculated Amplitudes[a]

	distance	l(GED)	l(calc)
C−H	1.11	0.077(6) l_1	0.080
N−Cl	1.41	0.043[b]	0.043
N−F	1.41	0.048[b]	0.048
N−C2	1.45	0.048[b]	0.048
F···H	2.02	0.106(7) l_2	0.107
N···H	2.07−2.14		0.099
C1···C2	2.38	0.072(3) l_3	0.068
N···F	2.39		0.069
C2···C2′	2.41		0.060
$(C\cdots H)_{gauche}$	2.58−2.74	0.141(27) l_4	0.157
$(F\cdots H)_{gauche}$	2.71−3.18	0.250[b]	0.248
C2···F	2.92	0.124(10) l_5	0.143
$(C\cdots H)_{trans}$	3.33−3.37	0.126(34) l_6	0.101
$(F\cdots H)_{trans}$	3.96	0.150[b]	0.151

[a] Values in Å, error limits are 3σ values. For atom numbering see Figure 3. [b] Not refined.

$^1/_3$[2(C1NC2) + (C2NC2′)], and the difference ΔCNC = (C1NC2) − (C2NC2′) were chosen as independent geometric parameters. ΔCNC was constrained to the ab initio MP2/6-311G(2d,p) value (1.5°) with an estimated uncertainty of ±0.5°. Local C_{3v} symmetry was assumed for the CH_3 groups with a tilt angle between the C_3 axis and the N−C bond distance. This tilt occurs toward the nitrogen lone pair and the angle was set to the ab initio value (2.2°) in the least-squares refinement. The HCH and NCH angles in the NCH_2F group were set equal to the respective values in the NCH_3 groups. If the ab initio values were used instead of this assumption, the refined parameters were almost identical to those in Table 1. Furthermore, the vibrational amplitudes for the bond distances N−C1, N−C2, and C−F were fixed at the spectroscopic values in order to avoid even larger correlations between these parameters. These amplitudes were calculated with the program NORCOR[18] from an approximate force field based on the valence force constants for trimethylamine.[19] The effect of the constraints for the bonded vibrational amplitudes was tested by changing the spectroscopic values by ±0.003 Å. The refined bond lengths varied by less than the respective error limits, which are three times the standard deviations of the least-squares analysis. Vibrational amplitudes for nonbonded distances were refined in groups and further assumptions are evident from Table 2. With these assumptions seven geometric parameters and six vibrational amplitudes were refined simultaneously. Despite the constraints described above, large correlations occur between some refined geometric parameters (Table 3). The results of the final least-squares analysis are given in Table 1 (geometric parameters p_i) and Table 2 (vibrational amplitudes l_k).

Discussion

As discussed in the introduction, the anomeric effect is expected to influence the conformational properties, i.e., the potential function for internal rotation around the $N-CH_2F$ bond, and bond lengths and bond angles. From the GED analysis we find that the global minimum of the potential function occurs for the antiperiplanar structure with ϕ(lpNCF) = 180°. For a synperiplanar ($\phi = 0°$) or synclinal ($\phi \approx 60°$) orientation, the peak at ca. 2.9 Å in the RDF, which corresponds to the C2···F and C2′···F distances, would either be shifted to a larger r value or be split into two peaks. We estimate from the GED data that the contribution of such a second conformer is less than 5%, which corresponds to a free enthalpy difference $\Delta G° > 2$ kcal mol^{-1}. A stable synclinal conformation of $CH_2FN(CH_3)_2$ is predicted by ab initio (HF/3-21G$^{(*)}$) and LDF (VWN/TZVP) calculations which is 4.5 or 5.3 kcal mol^{-1} higher in energy than the anti form and thus not detectable in a GED experiment. Since anti and synclinal structures differ by the bond type (C−F or C−H) which is oriented anti to the nitrogen lone pair, this energy difference corresponds closely to the difference between lp(N) → σ*(C−F) and lp(N) → σ*(C−H) interaction energies. The torsional barrier between the anti and synclinal conformations is predicted to be 9.0 kcal mol^{-1}, which is much higher than the usual barriers for $N-CH_3$ torsion of ca. 3 kcal mol^{-1}. The potential curve for $CH_2FN(CH_3)_2$ differs appreciably from that calculated for CH_2FNH_2. A detailed discussion of the conformational properties of the latter compound is given by Irvine et al.[8] Independent of the calculational method, no minimum is predicted for synclinal ($\phi \approx 60°$) orientation. Some ab initio methods predict a shallow minimum for the synperiplanar conformation ($\phi = 0°$), whereas other methods predict the inversion barrier to be lower than the syn structure. A similar dependence of the relative energies of synperiplanar structure and inversion barrier on the calculational method has also been observed for $CH_2FN(CH_3)_2$.

The influence of the anomeric effect is also reflected in bond lengths and bond angles of $CH_2FN(CH_3)_2$. This becomes evident from a comparison of trimethylamine and partially fluorinated derivatives (Table 4). The shortening of the N−C bond between $CH_3-N(CH_3)_2$ (1.458(1) Å) and $CF_3N(CH_3)_2$ (1.383(16) Å) can be attributed to two different effects, (1) lp(N) → σ*(C−F) interaction and (2) electrostatic attraction between the nitrogen and carbon net charges ($N^{-\delta}-C^{+\delta}$). Although it is not possible to separate these two effects strictly, their relative importance can be inferred from a comparison of N−C bond distances in $CH_2FN(CH_3)_2$ (1.408(13) Å) and $CF_3N(CH_3)_2$. In the latter compound where electrostatic attraction can be assumed to be roughly three times as strong, the bond shortens only by 0.02−0.03 Å. On the other hand, the combined effect of lp(N) → σ*(C−F) interaction and much weaker electrostatic attraction leads to a shortening of ca. 0.05 Å between $CH_3-N(CH_3)_2$ and $CH_2FN(CH_3)_2$. Thus, the anomeric effect appears to have a stronger influence on the bond length than the electrostatic attraction.

C−F bond lengths in fluoromethanes F−CXYZ are known to depend strongly on the electronegativity of the substituents X, Y, and Z,[20] and to decrease with increasing electronegativity. This trend has been rationalized by electrostatic interactions $F^{-\delta}-C^{+\delta}$. The long bond in $F-CH_2N(CH_3)_2$ (1.410(5) Å) which is even longer than that in $F-CH_3$ (1.391(1) Å[21]), despite the higher electronegativity of the $N(CH_3)_2$ group compared to that of hydrogen, can be rationalized by the no-bond−double-bond resonance which corresponds to the anomeric effect. This resonance structure also implies widening of the N−C−F and

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(18) Christen D. *J. Mol. Struct.* **1978**, *151*, 101.

(19) Fujiwara, H.; Egawa, T.; Konaka, S. *J. Mol. Struct.* **1995**, *344*, 217.

(20) Oberhammer H. In *The Chemistry of Halides, Pseudohalides and Azides;* Patai, S., Rappoport, Z., Eds.; John Wiley: New York, 1995; Suppl. D2, Part 1, pp 31−83.

(21) Egawa, T.; Yamamoto, S.; Nakata, M.; Kuchitsu, K. *J. Mol. Struct.* **1987**, *156*, 213.

Table 3. Correlation Coefficients (×100) of Least-Squares Analysis

p_1	100												
p_2	−96	100											
p_3	−98	97	100										
p_4	−5	4	8	100									
p_5	29	−29	−26	8	100								
p_6	−66	65	63	−4	−89	100							
p_7	−43	40	39	−15	−62	73	100						
l_1	−21	26	26	0	−5	13	5	100					
l_2	32	−32	−33	−5	−29	5	−13	−6	100				
l_3	24	−22	−20	12	49	−49	−54	2	7	100			
l_4	85	−83	−84	−6	23	−57	−42	−18	42	15	100		
l_5	65	−64	−64	−4	38	−57	−24	−15	9	14	70	100	
l_6	−8	8	7	−5	−38	31	17	0	13	−20	−5	0	100

Table 4. Skeletal Parameters of Trifluoromethylamine and Partially Fluorinated Derivatives

	$N-CH_{3-n}F_n$	$N-CH_3$	$\sum \alpha(N)^d$	$N-C-F_a{}^e$
$CH_3-N(CH_3)_2{}^a$	1.458(1)	1.458(1)	331.8(4)	
$CH_2F-N(CH_3)_2{}^b$	1.408(13)	1.466(9)	334.8(17)	115.9(24)
$CF_3-N(CH_3)_2{}^c$	1.383(16)	1.481(10)	336.8(14)	115.1(10)

[a] Reference 19. [b] This work. [c] Reference 12. [d] Sum of CNC bond angles. [e] F_a fluorine atom anti to nitrogen lone pair.

C−N−C angles. The N−C−F angle is indeed much larger than tetrahedral (115.9(24)°). A similar angle to the fluorine atom in the anti position has been reported for $CF_3N(CH_3)_2$ (115.1(10)°). The sum of the C−N−C angles increases slightly with fluorination, but the large experimental uncertainties do not allow a definite conclusion.

The bond lengths and bond angles obtained from low-level (HF/3-21G$^{(*)}$) and high-level (Mp2/6-311G(2d,p)) ab initio calculations differ by less than 0.01 Å and 1.5°, respectively, and both methods reproduce the experimental values very well. If we consider the systematic differences between the vibrationally averaged GED distances (r_a) and the calculated equilibrium distances (r_e), which are estimated to be 0.005−0.010 Å for bonds between heavy atoms and 0.015−0.020 Å for C−H bonds, the Mp2/6-311G(2d,p) bond lengths agree extremely well with the experimental bond lengths. The LDF method predicts all bond lengths by ca. 0.02 Å too short, except for the C−F bond where the calculated value is ca. 0.02 Å too long. All theoretical methods reproduce the bond angles better than 3°.

Experimental Section

(Fluoromethyl)dimethylamine was prepared by cleavage of bis(dimethylamino)methane with 1-fluoro-2,4-dinitrobenzene in nitrobenzene, following a procedure given by Böhme et al.[10] Fractional distillation yielded a fraction (bp 45−47 °C) containing 93% (GC) (fluoromethyl)dimethylamine, whose ^1H- and ^{19}F-NMR spectra were in accordance with reported data.[22,23] (Fluoromethyl)dimethylamine is a volatile, stable liquid[10] which slowly attacks glass under open air.

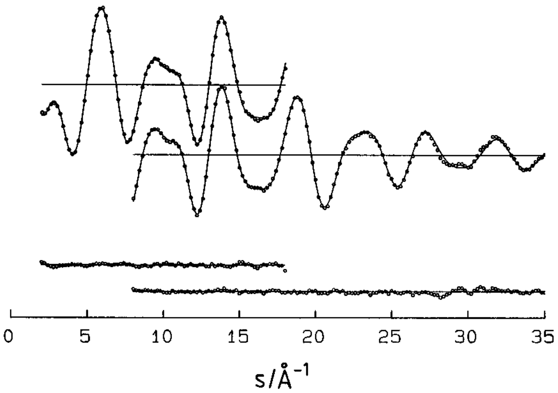

Figure 4. Experimental (dots) and calculated (full line) molecular scattering intensities for long (above) and short (below) nozzle-to-plate distances and differences.

The sample was redistilled before the GED experiment and no impurities could be detected in the gas infrared spectrum, which was recorded under the same condition as the GED experiment (see below). The GED intensities were measured with a Gasdiffractograph[24] at 25 and 50 cm nozzle-to-plate distances and with an accelerating voltage of ca. 60 kV. The electron wavelength was calibrated with ZnO powder. The sample reservoir was cooled to −35 °C (ca. 15 Torr vapor pressure) and the inlet nozzle was at room temperature. The camera pressure did not exceed 10^{-5} Torr during the experiment. The photographic plates (Kodak Electron Image, 18 × 13 cm) were analyzed by the usual methods.[25] Averaged molecular scattering intensities in the s-ranges 2−18 and 8−35 Å^{-1} ($s = (4\pi/\lambda)\sin(\theta/2)$, λ electron wavelength, θ scattering angle) in intervalls of $\Delta s = 0.2$ Å^{-1} are shown in Figure 4.

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(22) Böhme, H.; Sickmüller, A. *Chem. Ber.* **1977**, *110*, 208.

(23) Brauer, D. J.; Bürger, H.; Grunwald, M.; Pawelke, G.; Wilke, J. *Z. Anorg. Allg. Chem.* **1986**, *537*, 63.

(24) Oberhammer, H. *Molecular Structure by Diffraction Methods;* The Chemical Society, Burlington House: London, 1976; Vol. 4, p 24.

(25) Oberhammer, H.; Gombler, W.; Willner, H. *J. Mol. Struct.* **1981**, *70*, 273.