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Dixanthylurea (N, N′-di-9H-Xanthen-9-ylurea)

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$C_{27}H_{20}N_2O_3$, MW = 420, orthorhombic, $Pbc2_1$, a = 4.686(2), b = 16.784(8), c = 25.924(10)Å, V = 2039Å^3, d_{obs} = 1.37 g cm^{-3} (flotation), d_{calc} = 1.369g cm^{-3}, Z = 4. The structure has been determined by direct methods and refined to R = 0.045 based on 1419 independent reflections. No crystallographic symmetry element is present in the dixanthylurea molecule. In fact, the molecule is considerably distorted from any possible mirror symmetry. The molecules are hydrogen bonded in an infinite chain along the *a*-axis. The compound is of interest because of its role in the analytical determination of urea.

Key words: Crystal structure; molecular structure; single crystal x-ray diffraction; standard test; urea complex; urea in sera.

1. Introduction

Dixanthylurea was prepared by the procedure of Fosse [4].[1] A solution of urea in aqueous acetic acid was mixed with a solution of xanthydrol in methanol. The crude product was recrystallized from dimethyl sulfoxide. The sample was dried at 140 °C; M.P. 283–285 °C. Anal calc. for $C_{27}H_{20}N_2O_3$: C, 77.13; H, 4.79; N, 6.66. Found: C, 77.36; H, 4.89; N, 6.76.

The unit cell parameters were determined from a least-squares refinement of 15 reflections measured on a 4-circle diffractometer. The density (flotation) was consistent with $C_{27}H_{20}N_2O_3$ and $Z = 4$. On the basis of the systematic extinctions observed on the diffractometer, the space group was determined to be Pbcm(centric) or $Pbc2_1$ (acentric). A successful solution could be found only with the acentric space group.

A clear platelike crystal (0.29 × 0.14 × 0.04mm) was used for data collection. 1419 unique reflections were measured on an automated 4-circle diffractometer out to $\theta = 57.3°$ using the bisecting mode, θ–2θ scans, CuKα radiation (λ = 1.54178Å) which was monochromated with a pyrolytic graphite crystal. Three reflections, measured periodically, showed no significant decrease in intensity during data collection. The data were corrected for Lorentz and polarization effects but not for absorption (μ = 6.8cm^{-1}).

The trial model containing all atoms of the molecule was obtained with the program MULTAN [5]. The structure solution was obtained by the sequence: trial model, isotropic refinement, difference map, block matrix anisotropic refinement. The approximate position of the hydrogen atom on each nitrogen was determined from a difference map. In the refinement, however, these positions were calculated, as were the benzenoid hydrogen atoms, assuming trigonal geometry and a bond length of 1Å. The hydrogen atoms attached to C(2) and C(3) were calculated assuming tetrahedral geometry and a bond length of 1Å.

The weighting scheme applied was based on counting statistics combined with an instrumental instability factor. The weights were $1/\sigma(\mathrm{Fo})^2$ where $\sigma(Fo) = [Fo^2 + \sigma(I)/Lp]^{1/2} - Fo$ and $\sigma(I)^2 = I + 0.762 \times 10^{-4} I^2$. An extinction parameter was not used. Of the 1419 observed reflections, 1303 were used in the least-squares refinement. The 116 reflections indistinguishable from the background were not contributing reflections to the refinement but are included in the R values. The scattering factors for hydrogen were taken from Stewart, Davidson, and Simpson [15]; the scattering factors for C, O, N were computed from numerical Hartree-Fock wave functions [2]. The computer programs used were from XRAY 76 [14].

The model was refined to a conventional R, based on F, of 0.045 and a weighted R_w of 0.035

$$(R_w = [\Sigma w(F_o - |F_c|)^2 / \Sigma w F_o^2]^{1/2}).$$

The function minimized was $\Sigma w(F_o - |F_c|)^2$ with $w = [\sigma(F_o)]^{-2}$. The average and maximum shift/error on the last

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Figures in brackets indicate the literature references at the end of this paper.

cycle of refinement were 0.27 and 1.69, respectively. An analysis of the difference map showed no peak greater than 0.15e $Å^{-3}$. Tables 1 and 2 list the final atomic parameters.

2. Discussion

On account of the biological importance of urea, methods to determine it have received much attention. Three methods are in general use: in one method, urea is hydrolyzed to ammonia and carbon dioxide using urease. The ammonia is then titrated with standard acid [8]. In another method, small amounts of urea are determined spectrophotometrically (or colorimetrically) using either Nessler's reagent (alkaline mercury potassium iodide) or following the reaction with diacetyl monoxime [3, 10, 11], diacetyl [9], or cyclohexane-1,2-dione dioxime (fluorescence spectra) [12] in strong acid media. In a third method, urea forms the very insoluble dixanthylurea when treated with a solution of xanthydrol (9H-xanthen-9-ol) in methyl alcohol in the presence of glacial acetic acid [4]. The insoluble precipitate may be estimated gravimetrically [4], colorimetrically [1] or as microcapillary columns of the dixanthylurea sediment [13].

A possible new method for urea determination, based on dixanthylurea isotope-dilution mass spectrometry, is being evaluated at NBS in the Organic Analytical Research Division. In work on this method, it was found necessary to accurately characterize, by single crystal X-ray diffraction, the molecular parameters of dixanthylurea.

TABLE 1. *Positional ($\times 10^4$) and thermal ($Å^2 \times 10^4$) parameters of the non-hydrogen atoms. The form of the thermal correction is:*

$$T = \exp[-2\pi^2(a^{*2}h^2U_{11} + b^{*2}k^2U_{22} + c^{*2}l^2U_{33} + 2a^*b^*hkU_{12} + 2a^*c^*hlU_{13} + 2b^*c^*klU_{23})]$$

		X	Y	Z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
	O_1	−1979(4)	8800(2)	2056(2)	286(12)	1005(20)	514(13)	4(20)	−7(21)	−257(13)
	O_2	4506(8)	9913(2)	3783(1)	1022(26)	923(23)	592(19)	−84(22)	−324(20)	−108(18)
	O_3	4788(7)	7741(2)	361(1)	661(20)	879(21)	487(16)	47(18)	170(16)	−96(17)
	N_1	2210(6)	9093(2)	2458(1)	352(19)	806(22)	332(19)	52(19)	−11(19)	−239(18)
	N_2	2242(7)	8488(2)	1678(1)	316(18)	701(21)	446(20)	−57(19)	14(19)	−216(18)
	C_1	658(7)	8798(3)	2061(2)	446(20)	586(21)	326(15)	59(32)	48(37)	−62(16)
	C_2	959(8)	9539(2)	2893(1)	391(21)	725(28)	390(20)	103(23)	12(18)	−163(20)
	C_3	1029(8)	8069(2)	1232(1)	421(22)	602(24)	355(18)	−96(21)	−15(19)	−133(19)
	C_1	2519(8)	10312(2)	2963(1)	486(24)	646(26)	414(20)	104(23)	−33(22)	−148(20)
	C_2	2332(10)	10916(3)	2597(2)	758(32)	865(33)	589(26)	−40(31)	−82(26)	−30(26)
	C_3	3759(12)	11616(3)	2645(2)	923(41)	772(35)	912(37)	−76(32)	25(34)	17(31)
R1	C_4	5553(12)	11726(3)	3051(2)	852(39)	772(35)	936(36)	−117(32)	223(37)	−163(32)
	C_5	5814(11)	11147(3)	3438(2)	741(34)	960(37)	721(30)	−120(34)	−79(32)	−328(30)
	C_6	4231(9)	10453(3)	3384(2)	608(28)	784(30)	512(25)	24(28)	−34(26)	−142(24)
	C_1	1001(9)	9052(2)	3384(1)	507(24)	678(26)	426(22)	121(24)	42(22)	−157(21)
	C_2	−696(11)	8380(3)	3443(2)	757(32)	786(30)	587(27)	−37(29)	12(28)	−127(26)
	C_3	−648(13)	7933(3)	3888(2)	965(41)	824(36)	810(34)	11(33)	149(36)	97(32)
R2	C_4	1110(15)	8148(4)	4282(2)	1266(51)	914(41)	613(32)	253(41)	113(36)	119(31)
	C_5	2796(12)	8800(3)	4240(2)	1087(45)	996(39)	466(26)	242(39)	−159(31)	−34(28)
	C_6	2746(10)	9257(3)	3789(2)	709(31)	718(28)	449(24)	132(28)	−12(25)	−113(23)
	C_1	1148(8)	8576(2)	746(1)	472(24)	626(26)	385(20)	−110(22)	9(20)	−135(20)
	C_2	−598(10)	9237(3)	690(2)	660(29)	739(28)	532(24)	−16(27)	37(25)	−48(24)
	C_3	−462(11)	9711(3)	255(2)	810(35)	739(31)	692(30)	19(31)	−66(30)	16(26)
R3	C_4	1432(12)	9522(3)	−133(2)	972(41)	827(36)	550(27)	−151(32)	−11(29)	104(28)
	C_5	3164(11)	8866(3)	−91(2)	829(37)	1032(39)	466(27)	−162(34)	103(26)	−38(28)
	C_6	2979(9)	8392(3)	347(2)	538(26)	739(28)	446(23)	−118(26)	47(22)	−117(23)
	C_1	2557(8)	7294(2)	1147(1)	435(24)	612(25)	467(22)	−31(24)	−73(21)	−119(19)
	C_2	2227(10)	6675(3)	1497(2)	761(32)	745(30)	629(27)	26(29)	98(27)	−1(24)
	C_3	3754(12)	5964(3)	1440(2)	1103(42)	676(31)	741(33)	51(32)	−18(34)	−7(26)
R4	C_4	5502(12)	5872(3)	1016(2)	816(38)	861(36)	754(32)	158(32)	−60(31)	−239(30)
	C_5	5838(11)	6470(3)	676(2)	644(30)	866(36)	585(27)	84(31)	−12(26)	−222(28)
	C_6	4358(10)	7174(2)	732(2)	558(26)	724(28)	409(22)	−75(26)	−18(24)	−210(23)

TABLE 2. *Positional parameters ($\times 10^3$) of the hydrogen atoms.*
For each hydrogen atom a fixed isotropic thermal parameter of $U = 0.080 Å^2$ of the form $\exp(-8\pi^2 U \sin^2\theta/\lambda^2)$ was assumed.

		X	Y	Z
	H(N1)	432	900	245
	H(N2)	436	856	169
	H(C2)	−108	967	282
	H(C3)	−102	795	130
	H2	114	1083	228
	H3	347	1205	239
R1	H4	673	1222	306
	H5	710	1123	374
	H2	−196	821	315
	H3	−191	745	394
R2	H4	118	783	460
	H5	410	895	453
	H2	−196	938	97
	H3	−176	1018	22
R3	H4	157	988	−44
	H5	453	873	−37
	H2	91	674	180
	H3	357	553	170
R4	H4	655	536	96
	H5	719	641	38

Bond distances and angles for dixanthylurea are given in figure 1. A stereoview of the molecule is shown in figure 2. There is a considerable difference between the nitrogen to carbon bond lengths. For example, N(1)-C(1) is 1.355(6)Å and N(1)-C(2) is 1.475(5)Å. A similar difference was observed in monomethylurea [6]. These bond distances indicate that partial double bond character exists between N(l)-C(l) and N(2)-C(l) with resonance in the planar

O
|:
N(1)--C(1)--N(2).

moiety.

In the molecule of dixanthylurea there are a number of other planar components. To assist in forming a visual picture of the molecule it is helpful to consider the angles that these planes make with one another. Table 3 shows that the four benzenoid rings and the urea group are planar and table 4 shows the angles that the various planes make with each other. There is no crystallographic symmetry element within the molecule of dixanthylurea. In fact, from the various figures (especially fig. 4), it can be clearly seen that there is considerable deviation from any possible mirror symmetry that could relate the left and the right side of the molecule.

The packing in the structure is illustrated in figure 3. Molecules of dixanthylurea are hydrogen bonded one to another to form infinite chains along the *a*-axis. The hydrogen bonding within each chain is illustrated in figure 4 which shows that the oxygen atom of one molecule is hydrogen bonded to two nitrogen hydrogen atoms of an adjacent molecule. The O(1). . .N(1) and the O(1). . .N(2) oxygen to nitrogen distances are 2.957 and 2.928Å, respectively. A similar type of hydrogen bonding and N. . .O distances were found in the packing of monomethylurea [6] and in phenylurea [7]. In addition to the 2:1 complex dixanthylurea, the 1:1 complex has been prepared.

We thank Vicky Himes for technical help. The figures were drawn using a local version of the ORTEP program of C. K. Johnson. The X-ray structure determination described in this paper was supported by the Food and Drug Administration, FDA-NBS Interagency Agreement 224758253.

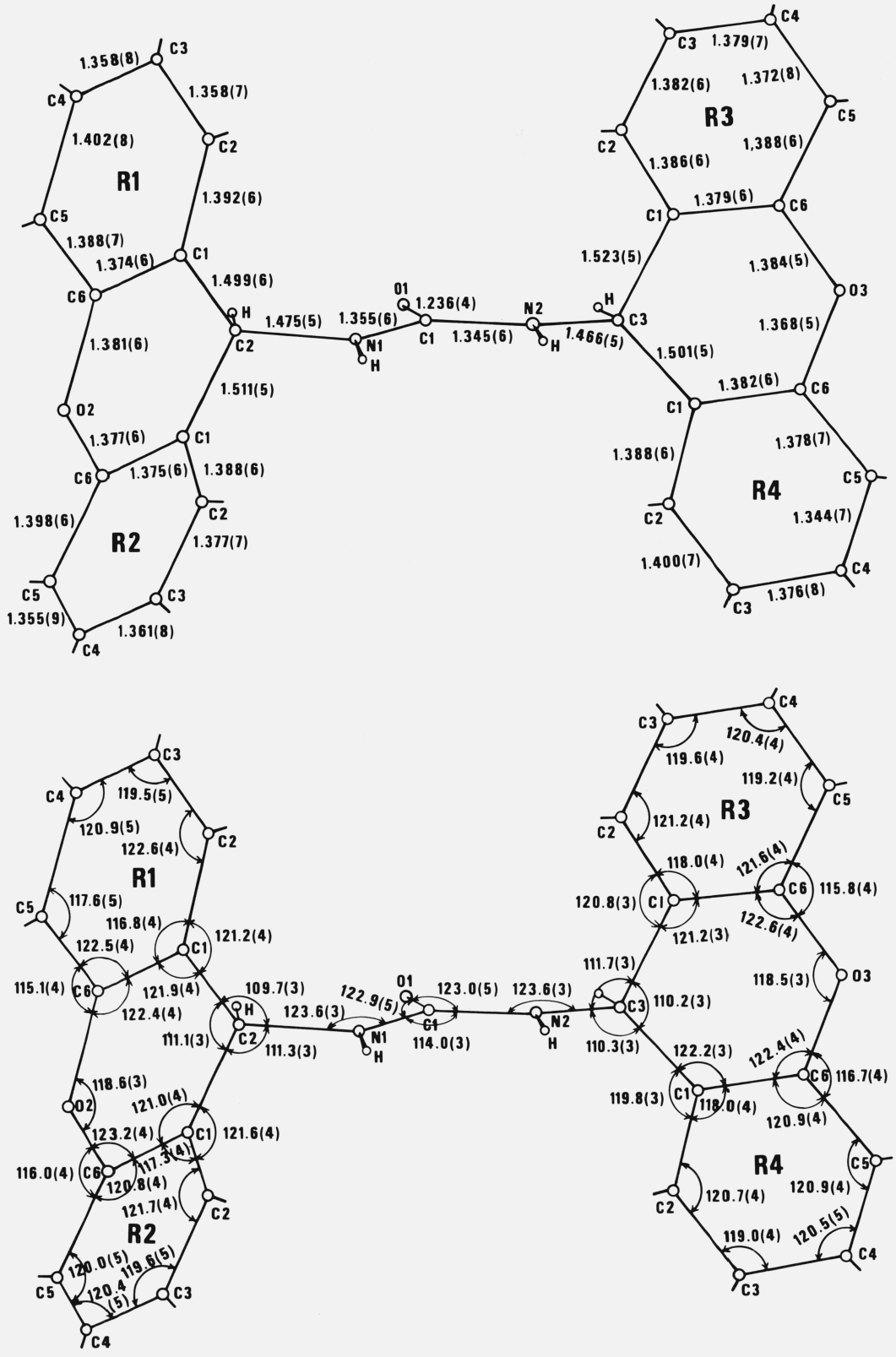

FIGURE 1. *Bond distances and angles.*

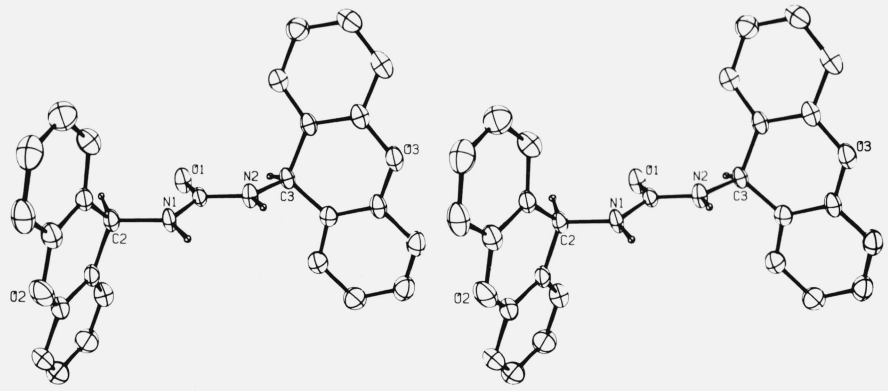

FIGURE 2. *Stereoview showing thermal motion.*

TABLE 3. *Summary of the results of the least-squares plane analyses.*

Urea Group	Delta	Ring 1 [a] (R1)	Delta	Ring 2 (R2)	Delta	Ring 3 (R3)	Delta	Ring 4 (R4)	Delta
C(1)	0.002	C1(R1)	−0.013	C1(R2)	−0.001	C1(R3)	0.010	C1(R4)	0.005
O(1)	−.007	C2(R1)	−.008	C2(R2)	.000	C2(R3)	−.003	C2(R4)	−.009
N(2)	.044	C3(R1)	.022	C3(R2)	.002	C3(R3)	−.004	C3(R4)	.012
N(1)	−.060	C4(R1)	−.017	C4(R2)	−.002	C4(R3)	.004	C4(R4)	−.012
C(2)	.034	C5(R1)	−.003	C5(R2)	.000	C5(R3)	.003	C5(R4)	.008
C(3)	−.013	C6(R1)	.018	C6(R2)	.001	C6(R3)	−.010	C6(R4)	−.005

[a] For rings R1, R2, R3, and R4, the least-squares plane is calculated through the six ring atoms. See figure 1 for atom and ring numbering.

TABLE 4. *Angles between the normals of the least-squares planes of the four benzenoid rings (of the two dixanthydryl groups) and the urea group*.[a]

Ring No.	R1	R2	R3	R4	Urea Group
R1	—	11°	85°	81°	84°
R2	11°	—	88°	82°	73°
R3	85°	88°	—	13°	73°
R4	81°	82°	13°	—	86°

[a] The angles are given to the nearest degree. See Table 3 and Figure 1 for the ring and group definitions.

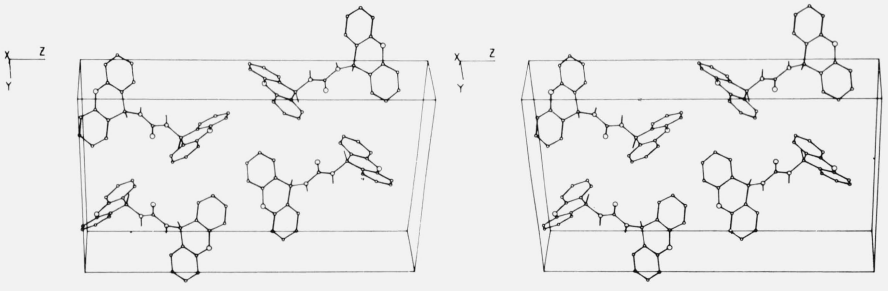

FIGURE 3. *Stereoscopic view of the structure.*

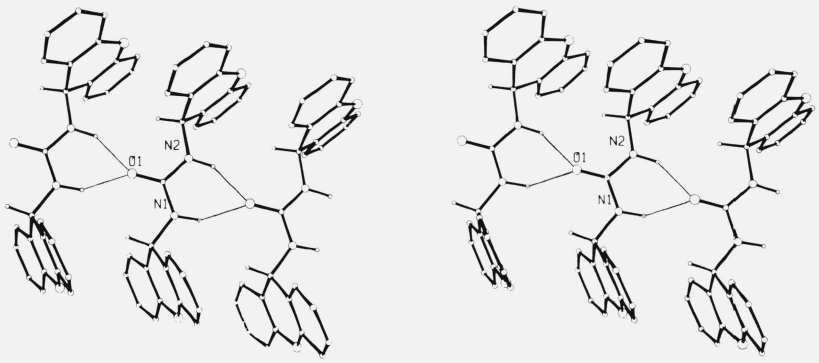

FIGURE 4. *Hydrogen bonding.*
The N(2)...O(1) and the N(1)...O(1) distances are 2.928 and 2.957Å, respectively.

3. References

[1] Allen, F. W., Luck, J. M., J. Biol. Chem. **82**, 693 (1929).

[2] Cromer, D. T. and Mann, J. B., Acta. Cryst. **A24**, 321-324 (1968).

[3] Fearon, W. R., Biochem. J. **33**, 902 (1939).

[4] Fosse, M. R., Compt. Rend. **154**, 1187 (1912); Ibid. **157**, 948 (1913); Ibid., **158**, 1076, 1588 (1914); Ibid; **159**, 253 (1914).

[5] Germain, G., Main, P., and Woolfson, M. M., Acta Cryst. **A27**, 368-376. (1971).

[6] Huiszoon, C. and Tiemessen, G. W. M., Acta Cryst. **B32**, 1604-1606. (1976)

[7] Kashino, S. and Haisa, M., Acta Cryst. **B33**, 855-860. (1977).

[8] Marshall, E. K., J. Biol. Chem. **15**, 487-495. (1913).

[9] Natelson, S., Scott, M. L., Beffa, C., Amer. J. Clinic. Path. **21**, 275. (1951).

[10] Ormsby, A. A., J. Biol. Chem. **146**, 595. (1942).

[11] Osinski, T. and Sosnowski, J., Chem. Anal. (Warsaw) **12**, 1191 (1967); Chem. Abstr., **68**, 66268 (1968).

[12] Panek, E., Siest, G., Bull. Soc. Pharm Nancy., 37-40 (1967); Chem. Abstr., **69**, 6847 (1968).

[13] Searcy, R. L., Korotzer, J. L., Douglas, G. L., Berquist, L. M., Clin. Chem., **10**, 128, (1964).

[14] Stewart, J. M., Machin, P. A., Dickinson, C. W., Ammon H. L., Heck, H., and Flack, H., The XRAY System-Version of March 1976, Tech. Rep. TR-446, Computer Science Center, University of Maryland, College Park, Maryland (1976).

[15] Stewart, R. F., Davidson, E. R. and Simpson, W. T., J. Chem. Phys. **42**, 3175-3187. (1965).