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References

GNANAGURU, K., RAMASUBBU, N., VENKATESAN, K. & RAMAMURTHY, V. (1985). *J. Org. Chem.* **50**, 2337–2346.
LOGUNOV, O. A., STARTSEV, A. V. & STOILOV, YU. YU. (1981). *Kvantovaya Elektron. (Moscow)*, **6**, 1307–1310.
MASILAMANI, V. (1987). ICTP Internal Report No. IC/87/109. Trieste, Italy.
MASILAMANI, V., CHANDRASEKAR, V., SIVARAM, B. M., SIVASANKAR, B. & NATARAJAN, S. (1986). *Opt. Commun.* **59**, 203–207.
MASILAMANI, V., SASTIKUMAR, D., NATARAJAN, S. & NATARAJAN, P. (1987). *Opt. Commun.* **62**, 389–395.
MESSAGER, J. C. & DELUGEARD, Y. (1974). *Cryst. Struct. Commun.* **3**, 391–396.
MURTHY, G. S., RAMAMURTHY, V. & VENKATESAN, K. (1988). *Acta Cryst.* C44, 307–311.
NARDELLI, M. (1983). *Comput. Chem.* **7**, 95–98.
SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.
SHELDRICK, G. M. (1986). *SHELX*86. Program for crystal structure solution. Univ. of Göttingen, Federal Republic of Germany.
TUCCIO, S. A., DREXHAGE, K. H. & REYNOLDS, G. A. (1973). *Opt. Commun.* **7**, 248–252.

Structure of α-D-N-Acetyl-1-O-methylneuraminic Acid Methyl Ester

BY H. KOOIJMAN, L. M. J. KROON-BATENBURG AND J. KROON

Laboratorium voor Kristal- en Structuurchemie, Rijksuniversiteit, Padualaan 8, 3584 CH Utrecht, The Netherlands

J. N. BREG

Department of Bio-Organic Chemistry, Rijksuniversiteit, Padualaan 8, 3584 CH Utrecht, The Netherlands

AND J. L. DE BOER

Department of Inorganic Chemistry, University of Groningen, Nijenborgh 16, 9747 AG Groningen, The Netherlands

Abstract. $C_{13}H_{23}NO_9$, $M_r = 337.33$, orthorhombic, $P2_12_12_1$, $a = 8.8479$ (9), $b = 9.691$ (2), $c = 18.121$ (4) Å, $V = 1553.8$ (5) Å^3, $Z = 4$, $D_x = 1.442$ Mg m^{-3}, $\lambda(Mo\ K\alpha) = 0.71073$ Å, $\mu(Mo\ K\alpha) = 0.11$ mm^{-1}, $F(000) = 720$, $T = 100$ K, final $R = 0.034$ for 3398 observed diffractometer data. The conformation of the glycerol side chain is the same as in the structures of the two β forms of N-acetylneuraminic acid. The crystal consists of a two-dimensional network of hydrogen-bonded molecules and in the third direction there are only hydrophobic contacts.

Introduction. Sialic acids frequently occur as α-glycosidically linked terminal groups of carbohydrate chains in glycoproteins and glycolipids (Corfield & Schauer, 1982). The large range of their biological activity includes, for example, (anti)recognition of low- and high-molecular-weight compounds, influence on transport processes, hormone action, cellular adhesiveness and the life span of glycoproteins (Reuther, Köttgen, Bauer & Gerok, 1982). For these biological functions the charge and the conformation of the molecules are essential features.

N-Acetylneuraminic acid is one of the most frequently occurring sialic acids. So far only the crystal structures of two β-glycosidical forms, β-D-N-acetylneuraminic acid dihydrate (βNeu5Ac; Flippen, 1973) and β-D-N-acetylneuraminic acid methyl ester monohydrate (1MeβNeu5Ac; O'Connell, 1973) have been determined. It is of interest to study the α-glycosidic form of neuraminic acid because it is this form that occurs in nature, and effects on the conformation with respect to the β forms can be expected by the axial position of the carboxyl group. Therefore, we here report the crystal and molecular structure of α-D-N-acetyl-1-O-methylneuraminic acid methyl ester (1,2diMeαNeu5Ac). Because the intra-

and intermolecular hydrogen-bonding scheme is of major interest the experiment has been performed at low temperature in order to locate H atoms.

Experimental. Colourless transparent block-shaped crystals ($0.18 \times 0.10 \times 0.10$ mm), obtained by vapour diffusion of a solution in methanol against diethyl ether. Enraf–Nonius CAD-4 diffractometer, temperature 100 K, Mo $K\alpha$ radiation, graphite monochromator, lattice dimensions determined using 22 reflections in θ range 21 to 23°; the space group was established by observed systematic absences $h00$ with $h = 2n + 1$, $0k0$ with $k = 2n + 1$ and $00l$ with $l = 2n + 1$. $\omega/2\theta$ scan mode, scan width $(0.75 + 0.35 \tan\theta)°$, $2\theta_{max} = 56°$, $h = -11$ to 11, $k = 0$ to 12, $l = -23$ to 23; 7926 reflections measured, $R_{int} = 0.03$ from merging 3750 equivalent pairs; 3398 above $2.5\sigma(I)$ level. Three periodically measured standard reflections ($10\bar{6}$, 106, $\bar{1}23$) showed no significant decay in intensity during data collection, only slight absorption noticed ($< 10\%$ in ψ scan) and not corrected for, Lp correction. Structure solved by direct methods (SHELXS84; Sheldrick, 1984). Refinement on F by full-matrix least squares (SHELX76; Sheldrick, 1976) with anisotropic temperature factors for all non-H atoms. All H atoms could be located from a three-dimensional difference Fourier map; their positions and one common thermal parameter were subsequently refined. Scattering factors were taken from Cromer & Mann (1968), anomalous-dispersion corrections from Cromer & Liberman (1970). Convergence at $R = 0.034$, $wR = 0.030$ where $w = 1/\sigma^2(F_o)$. Max. and min. densities in final difference synthesis were 0.46 and -0.33 e Å^{-3} respectively. $\Delta/\sigma = 0.004$ (av.) and 0.052 (max.)

Discussion. The final atomic positional and isotropic thermal parameters are given in Table 1.* The molecular conformation and atomic numbering is shown in Fig. 1. Bond distances, bond angles and relevant torsion angles for non-H atoms are listed in Table 2. The geometric calculations were performed with the EUCLID package (Spek, 1982). Bond distances and angles are similar to those found in other saccharides (Arnott & Scott, 1972) although some peculiarity occurs in the anomeric region. Arnott & Scott (1972) and Jeffrey, Pople, Binkley & Vishveshwara (1978) have studied the changes in geometry near the anomeric centre for the various anomers, by crystal-structure statistics and by theoretical methods. In line with their observations, the

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* Lists of structure factors and anisotropic thermal parameters and complete geometrical data have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 52346 (28pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Final coordinates and equivalent isotropic thermal parameters* (Å^2) *with their e.s.d.'s in parentheses for non-*H *atoms and selected* H *atoms for* 1,2diMeαNeu5Ac

	x	y	z	U_{eq}* or U_{iso}
O(1)	0.2357 (1)	0.2053 (1)	0.43000 (6)	0.0160 (3)
O(2)	0.1836 (2)	−0.1243 (1)	0.45918 (7)	0.0254 (4)
O(4)	−0.2655 (1)	−0.0717 (2)	0.33162 (7)	0.0310 (4)
O(6)	0.1985 (1)	−0.0225 (1)	0.34678 (5)	0.0146 (3)
O(7)	0.2824 (1)	−0.0680 (1)	0.19856 (6)	0.0150 (3)
O(8)	0.3569 (1)	0.2625 (1)	0.28858 (6)	0.0155 (3)
O(9)	0.6437 (1)	0.1990 (1)	0.21880 (8)	0.0249 (4)
O(11)	0.0696 (1)	0.1300 (1)	0.51476 (6)	0.0188 (3)
O(12)	0.0221 (1)	−0.1030 (1)	0.12256 (6)	0.0161 (3)
N(5)	−0.0978 (1)	0.0356 (1)	0.20495 (7)	0.0132 (4)
C(1)	0.1472 (2)	0.1201 (2)	0.45217 (8)	0.0148 (4)
C(2)	0.1194 (2)	−0.0214 (2)	0.41461 (8)	0.0171 (5)
C(3)	−0.0451 (2)	−0.0631 (2)	0.4047 (1)	0.0216 (5)
C(4)	−0.1238 (2)	−0.0038 (2)	0.33764 (9)	0.0182 (5)
C(5)	−0.0220 (2)	−0.0202 (2)	0.26983 (8)	0.0130 (4)
C(6)	0.1262 (2)	0.0534 (2)	0.28872 (8)	0.0125 (4)
C(7)	0.2424 (2)	0.0646 (2)	0.22711 (8)	0.0119 (4)
C(8)	0.3891 (2)	0.1316 (2)	0.25472 (9)	0.0142 (5)
C(9)	0.4988 (2)	0.1576 (2)	0.19229 (9)	0.0180 (5)
C(10)	0.1019 (2)	0.2530 (2)	0.55836 (9)	0.0197 (5)
C(11)	0.3410 (3)	−0.1042 (2)	0.4766 (1)	0.0308 (6)
C(12)	−0.0767 (2)	−0.0159 (2)	0.13687 (8)	0.0132 (4)
C(13)	−0.1816 (2)	0.0379 (2)	0.0785 (1)	0.0172 (5)
H(14)	−0.283 (2)	−0.102 (2)	0.290 (1)	0.023 (1)
H(17)	0.204 (2)	−0.092 (2)	0.176 (1)	0.023 (1)
H(18)	0.324 (2)	0.255 (2)	0.332 (1)	0.023 (1)
H(19)	0.645 (2)	0.274 (2)	0.239 (1)	0.023 (1)
H(25)	−0.173 (2)	0.093 (2)	0.211 (1)	0.023 (1)

* $U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$

anomeric C—O bond length (1.403 Å) is shortened with respect to the average single C—O bond length in the title compound (1.429 Å). These authors also found that the difference in the two ring C—O bond lengths appears to be characteristic for the specific anomer, i.e. the bond involving the anomeric C atom is shorter when the anomeric C—O bond is in the axial position. In normal D-hexopyranoses this corresponds to the α anomer, but because C(8) is the reference atom for the D configuration in Neu5Ac, and C(6) has the L-*glycero* configuration, the axial position of the anomeric C—O bond corresponds to the β anomer. Thus one would expect the C(2)—O(6) and C(6)—O(6) bonds to be nearly equal in 1,2diMeαNeu5Ac but C(2)—O(6) appears to be shorter by 0.02 Å. Moreover, for β-D-hexoses, the O—C—O angle at the anomeric C atom appears to be narrow (average 107.3°) and the ring C—O—C angle appears to be 111.6° on the average (Arnott & Scott, 1972). The value of 107.1° for O(2)—C(2)—O(6) in 1,2diMeαNeu5Ac is in good agreement with the above, but the value of 114.4° for C(2)—O(6)—C(6) is unusually large and close to what is common for α-hexoses. Thus it seems that the geometrical features in the anomeric region are not so characteristic for the specific anomer when a carboxyl group is attached to the anomeric C atom.

The ring has the normal $^2C_5$ shape, somewhat distorted toward a $^6H_5$ half-chair conformation with puckering parameters $Q = 0.577$ (2) Å, $\theta = 162.2$ (2) and $\varphi = 92.2$ (2)° (Cremer & Pople, 1975). Comparison with the puckering parameters for 1MeβNeu5Ac ($Q = 0.540$ Å, $\theta = 176.0$, $\varphi = 212.9°$) and βNeu5Ac ($Q = 0.567$ Å, $\theta = 177.3$, $\varphi = 89.0°$) shows that due to the axial position of the carboxyl group the ring in the α form is more distorted.

It is of interest to compare the conformations of the carboxyl group, the N-acetyl group and the glycerol side chain for the three N-acetylneuraminic acids. The relevant torsion angles can be found in Table 2. The C=O bond of the carboxyl group is approximately coplanar with the ring C—O bond in 1,2diMeαNeu5Ac, whereas in both β compounds the C=O bond is found to be nearly eclipsed with the anomeric C—O bond. The preference for a planar conformation of the O—C—C=O fragment is also known to occur in α-hydroxy carboxylic acids (Kanters, Kroon, Peerdeman & Schoone, 1967; Kroon, 1982; Newton & Jeffrey, 1977). Due to the acetal group, two such fragments occur in neuraminic acids so that there are two alternatives for the planarity. In the α form the carboxyl group is probably not aligned with the anomeric C—O bond, as in the β compounds, because this would introduce steric repulsion with C(6)—H(6) and C(4)—H(4).

The N-acetyl group is essentially planar. The r.m.s. deviation of the atoms C(13), C(12), O(12) and N(5) from their least-squares plane is 0.001 Å, the deviation of atom C(5) from that plane is only 0.202 (5) Å. In all three neuraminic acids the N-acetyl group adopts the Z conformation of the peptide bond [C(12)=O(12) is eclipsed with N(5)—C(5)] and the N(5)—H(25) bond is in *trans* position to the ring C(5)—H(5) bond. In the latter torsional parameter differences of more than 20° occur which can be
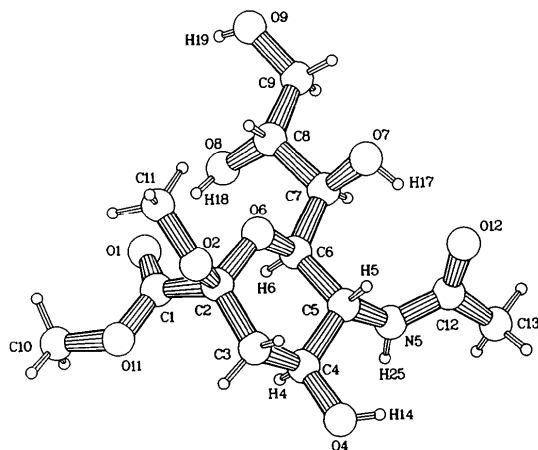

Fig. 1. Molecular conformation and atomic numbering of 1,2diMeαNeu5Ac.

Table 2. *Bond distances* (Å), *bond angles* (°) *and selected torsion angles* (°)

O(1)—C(1)	1.206 (2)	N(5)—C(12)	1.344 (2)
O(4)—C(4)	1.419 (2)	C(3)—C(4)	1.513 (2)
O(7)—C(7)	1.430 (2)	C(6)—C(7)	1.521 (2)
O(11)—C(1)	1.329 (2)	C(12)—C(13)	1.501 (2)
N(5)—C(5)	1.457 (2)	O(2)—C(11)	1.441 (3)
C(2)—C(3)	1.521 (2)	O(6)—C(6)	1.434 (2)
C(5)—C(6)	1.531 (2)	O(9)—C(9)	1.426 (2)
C(8)—C(9)	1.511 (2)	O(12)—C(12)	1.243 (2)
O(2)—C(2)	1.403 (2)	C(1)—C(2)	1.550 (2)
O(6)—C(2)	1.414 (2)	C(4)—C(5)	1.531 (2)
O(8)—C(8)	1.438 (2)	C(7)—C(8)	1.535 (2)
O(11)—C(10)	1.458 (2)		

C(2)—O(6)—C(6)	114.4 (1)	C(2)—O(2)—C(11)	114.9 (1)
C(1)—O(11)—C(10)	114.9 (1)	C(5)—N(5)—C(12)	122.6 (1)
O(1)—C(1)—O(11)	124.7 (2)	O(1)—C(1)—C(2)	124.2 (1)
O(11)—C(1)—C(2)	110.9 (1)	O(2)—C(2)—O(6)	107.1 (1)
O(2)—C(2)—C(1)	108.2 (1)	O(2)—C(2)—C(3)	105.4 (1)
O(6)—C(2)—C(1)	108.0 (1)	O(6)—C(2)—C(3)	111.6 (1)
C(1)—C(2)—C(3)	116.0 (1)	C(2)—C(3)—C(4)	115.7 (2)
O(4)—C(4)—C(3)	107.0 (1)	O(4)—C(4)—C(5)	114.2 (1)
C(3)—C(4)—C(5)	109.5 (1)	N(5)—C(5)—C(4)	109.8 (1)
N(5)—C(5)—C(6)	113.7 (1)	C(4)—C(5)—C(6)	106.0 (1)
O(6)—C(6)—C(5)	107.9 (1)	O(6)—C(6)—C(7)	105.8 (1)
C(5)—C(6)—C(7)	116.6 (1)	O(7)—C(7)—C(6)	111.6 (1)
O(7)—C(7)—C(8)	106.8 (1)	C(6)—C(7)—C(8)	111.3 (1)
O(8)—C(8)—C(7)	110.2 (1)	O(8)—C(8)—C(9)	107.4 (1)
C(7)—C(8)—C(9)	111.7 (1)	O(9)—C(9)—C(8)	111.8 (1)
O(12)—C(12)—N(5)	122.8 (1)	O(12)—C(12)—C(13)	121.6 (1)
N(5)—C(12)—C(13)	115.6 (1)		

	1,2diMeαNeu5Ac	1MeβNeu5Ac	βNeu5Ac
C(12)—N(5)—C(5)—C(4)	−148.3 (2)	−140.4	−125.2
C(5)—N(5)—C(12)—O(12)	−9.1 (2)	−5.1	−0.8
O(1)—C(1)—C(2)—O(6)	−7.8 (2)	93.6	128.4
C(5)—C(6)—C(7)—O(7)	−57.0 (2)	−49.0	−63.6
C(6)—C(7)—C(8)—O(8)	−54.4 (2)	−71.9	−71.1
C(7)—C(8)—C(9)—O(9)	−170.7 (1)	−176.9	−177.4

attributed to the intramolecular O(7)—H(17)···O(12) hydrogen bond which occurs in 1,2diMeαNeu5Ac and 1MeβNeu5Ac and produces a larger C(4)—C(5)—N(5)—C(12) torsion angle than in the case of βNeu5Ac where this hydrogen bond is absent.

The overall conformation of the glycerol side chain is the same for all three compounds as far as non-H atoms are concerned. In 1,2diMeαNeu5Ac, in addition to O(7)—H(17)···O(12), another intramolecular hydrogen bond involving the glycerol side chain is directed toward the carboxyl group [O(8)—H(18)···O(1)]. In the β forms this hydrogen bond cannot occur because of the equatorial position of the carboxyl group. As in the crystal structure of βNeu5Ac, neither of these hydrogen bonds occurs, the preference for this particular conformation of the glycerol side chain seems not to depend on intramolecular hydrogen bonding, although it is likely that in solution they will contribute to the rigidity of the molecule. The conformation of the glycerol side chain is consistent with ^3J coupling constants obtained by ^1H NMR measurements of βNeu5Ac in aqueous solution (Brown, Brey & Weltner, 1975) although in that paper another conformation is proposed. From T_1 relaxation times obtained from ^{13}C

Table 3. *Hydrogen-bond distances* (Å) *and angles* (°)
of 1,2*diMeαNeu*5*Ac*

	D—H	H···A	D···A	D—H···A	Symmetry operation*
O(4)—H(14)···O(8)	0·83 (2)	2·04 (2)	2·825 (2)	158 (2)	545·3
O(9)—H(19)···O(7)	0·81 (2)	2·01 (2)	2·787 (2)	160 (2)	655·3
N(5)—H(25)···O(9)	0·87 (2)	1·93 (2)	2·793 (2)	172 (2)	455·1
O(7)—H(17)···O(12)	0·84 (2)	1·88 (2)	2·704 (2)	167 (2)	555·1
O(8)—H(18)···O(1)	0·85 (2)	1·99 (2)	2·832 (2)	170 (2)	555·1

* The symmetry operation is performed on the acceptors (A). The first three digits specify the lattice translations. The last digit indicates one of the following symmetry operations: (1) x, y, z; (2) $\frac{1}{2} + x, \frac{1}{2} - y, -z$; (3) $-x, \frac{1}{2} + y, \frac{1}{2} - z$; (4) $\frac{1}{2} - x, -y, \frac{1}{2} + z$ (*e.g.* 545·3 is $-b$ from 555·3).
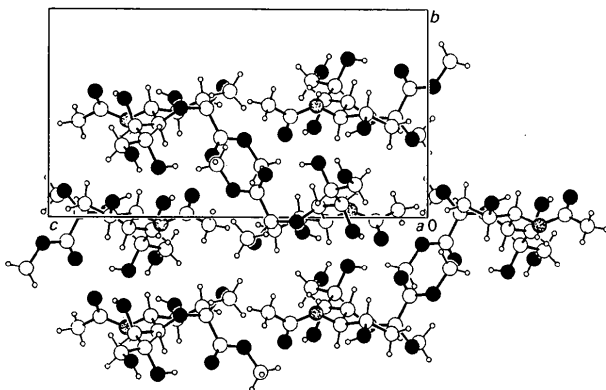

Fig. 2. View of the structure down the *a* axis. The C, O, N and H atoms are represented by white, black, dotted and small spheres, respectively.

NMR data (Czarniecki & Thornton, 1977) on α and β forms of Neu5Ac in aqueous solution, low mobility was found around the C(6)—C(7) and C(7)—C(8) bonds. The persistence of this particular glycerol side-chain conformation in crystals is in agreement with these findings.

The hydrogen-bonding geometries in the crystal structure of 1,2diMeαNeu5Ac are listed in Table 3. Every molecule is surrounded by six hydrogen-bonded neighbours. A two-dimensional network is formed by hydrogen bonds in the [100] and [110] directions. The contacts in the [001] direction are hydrophobic in nature. Fig. 2 gives a view of the structure down *a*.

References

ARNOTT, S. & SCOTT, W. E. (1972). *J. Chem. Soc. Perkin Trans.* 2, pp. 324–335.
BROWN, E. B., BREY, W. S. JR & WELTNER, W. JR (1975). *Biochim. Biophys. Acta*, **399**, 124–130.
CORFIELD, A. P. & SCHAUER, R. (1982). In *Sialic Acids, Cell Biology Monograph*, Vol. 10, edited by R. SCHAUER, Ch. B. Wien: Springer-Verlag.
CREMER, D. & POPLE, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
CROMER, D. T. & LIBERMAN, D. (1970). *J. Chem. Phys.* **53**, 1891–1898.
CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A**24**, 321–324.
CZARNIECKI, M. F. & THORNTON, E. R. (1977). *J. Am. Chem. Soc.* **99**, 8273–8279.
FLIPPEN, J. L. (1973). *Acta Cryst.* B**29**, 1881–1886.
JEFFREY, G. A., POPLE, J. A., BINKLEY, J. S. & VISHVESHWARA, S. (1978). *J. Am. Chem. Soc.* **100**, 373–379.
KANTERS, J. A., KROON, J., PEERDEMAN, A. F. & SCHOONE, J. C. (1967). *Tetrahedron*, **23**, 4027–4033.
KROON, J. (1982). In *Molecular Structure and Biological Activity*, edited by J. G. GRIFFIN & W. L. DUAX. New York: Elsevier Biomedical.
NEWTON, M. D. & JEFFREY, G. A. (1977). *J. Am. Chem. Soc.* **99**, 2413–2421.
O'CONNELL, A. M. (1973). *Acta Cryst.* B**29**, 2320–2328.
REUTHER, W., KÖTTGEN,E., BAUER, C. & GEROK, W. � '82). In *Sialic Acids, Cell Biology Monograph*, Vol. 10, edite.. by R. SCHAUER, Ch. J. Wien: Springer-Verlag.
SHELDRICK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.
SHELDRICK, G. M. (1984). *SHELXS84*. Program for crystal structure determination. Univ. of Göttingen, Federal Republic of Germany.
SPEK, A. L. (1982). *The EUCLID* package. In *Computational Crystallography*, edited by D. SAYRE, p. 528. Oxford: Clarendon Press.

Conformational Study of 1,3,5-Tris(*o*-chlorophenyl)-1,3,5-triazacyclohexane and 1,3,5-Tris(*p*-chlorophenyl)-1,3,5-triazacyclohexane

By AHCENE BOUCHEMMA, PETER H. MCCABE AND GEORGE A. SIM

Chemistry Department, University of Glasgow, Glasgow G12 8QQ, Scotland

Abstract. $C_{21}H_{18}Cl_3N_3$, $M_r = 418·80$. *o*-Chlorophenyl compound, orthorhombic, *Pnma*, $a = 20·899$ (4), $b = 12·466$ (3), $c = 7·372$ (1) Å, $V = 1921$ (1) Å^3, $Z = 4$, $D_x = 1·45$ Mg m^{-3}, λ(Mo $K\alpha$) $= 0·71069$ Å, $\mu = 0·49$ mm^{-1}, $F(000) = 864$, $T = 293$ K, $R = 0·040$ for 1581 independent observed reflections. *p*-Chloro-