

The Crystal and Molecular Structure of *N*-Methyl-2,4,6-trinitroacetanilide

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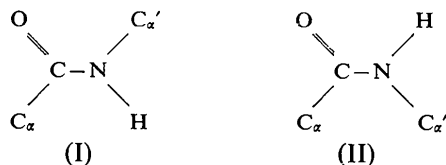
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N-Methyl-2,4,6-trinitroacetanilide ($C_8H_8N_4O_7$, *N*-acetyl-*N*-methyl-2,4,6-trinitroaniline or AM 246) forms crystals with the monoclinic space group $P2_1/c$ and with unit-cell constants $a = 7.813 \pm 0.002$, $b = 8.667 \pm 0.002$, $c = 17.990 \pm 0.001$ Å, and $\beta = 100.521 \pm 0.006^\circ$. There are four molecules per unit cell. The data were collected by the θ - 2θ scan technique on a G. E. XRD-5 diffractometer employing Ni-filtered $Cu K\alpha$ radiation. The structure was solved by the symbolic addition procedure and was refined by conventional least-squares and Fourier techniques to a final weighted R (based on F^2) of 0.027 for 2377 independent reflections. The acetyl group is in the *endo* conformation, with the carbonyl oxygen extending towards the aromatic ring. The nitro groups at the 2, 4, and 6 positions are rotated 54, 4, and 36° respectively, out of the plane of the benzene ring. The planar amide group is rotated 60° out of the plane of the aromatic ring. These rotations all have the same sense. The shortest intermolecular distances all appear to be normal van der Waals contacts except for a 'weak' hydrogen bond between the carbonyl oxygen and one of the picryl hydrogens of a neighboring molecule.

Introduction

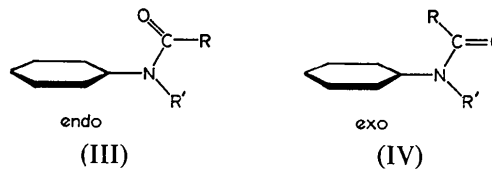
It is well known that the peptide linkage is essentially planar owing to the considerable π character in the C-N bond and that for steric reasons the *trans* conformation (I) is generally energetically preferred over the *cis* conformation (II) by a few kcal per mole.



Accordingly, the *cis* linkage is very unusual in a peptide. Although hindered rotation about the C-N bond is possible at normal temperatures, only a few examples of stabilized *cis*-linkages have been found (Hartsuk & Lipscomb, 1971; Konnert & Karle, 1969; Deber, Boven, Carver & Blout, 1970). Further knowledge of the circumstances under which one conformation is preferred over the other may be useful in understanding the folding of polypeptides in proteins.

N-Methyl-2,4,6-trinitroacetanilide is one of a series of anilides in which hindered rotation about the C-N bond has been studied by high resolution n.m.r. techniques (Weil, Blum, Heiss & Kinnaird, 1967; Pedersen & Pedersen, 1965; Fischer, 1968; Brown, Radom, Sternhill & Rae, 1968; Bourn, Gillies & Randall, 1966). Weil *et al.* concluded that the carbonyl group is *cis* to the benzene ring (*endo* conformation, III) rather than *trans* (*exo* conformation, IV) as it is in *N*-methylacetanilide (Pedersen & Pedersen, 1965). This study was undertaken in order to elucidate the

structural basis for the observed conformer stabilities in these compounds.



Experimental

Samples of *N*-methyl-2,4,6-trinitroacetanilide were obtained from Dr J. A. Weil, Argonne National Laboratory. The compound crystallizes from absolute ethanol solution as well formed polyhedra, transparent and pale yellow in color. Unit-cell parameters and optical data have been reported by Gebert, Fuchs & Christoph (1967); they are reproduced here in Table I for completeness. The space group was redetermined from precession photographs as $P2_1/c$ (extinctions: $h0l$ with l odd, $0k0$ with k odd). The crystal selected for the data collection was an irregular hexagonal prism 0.15 mm thick with an approximate diameter across the hexagonal face of 0.22 mm. The crystal was aligned with the unique axis coincident with the ϕ axis on a General Electric Single Crystal Orienter equipped with a proportional counter. Copper $K\alpha$ radiation ($\lambda = 1.54178$ Å) was used throughout. The take-off angle was 4°. All reflections with $2\theta < 145^\circ$ were measured by the θ - 2θ scan technique, using 10 sec background counts on each side of the scan. The scan width was 2.67° and the scan rate was 4° per min in 2θ . Layers of Ni foil were used both as β -filter and as attenuators. Three check reflections were measured periodically during the data collection to monitor the condition and alignment of the crystal. The $0kl$ zone was collected twice, once at the beginning of the data collection, and once at the end of the data collection as the equivalent zone $0k\bar{l}$. 2377 independent reflections

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were measured; of these, 184 had net intensities of zero or less.

Table 1. *Crystallographic and optical data*

$a = 7.813 \pm 0.002 \text{ \AA}$	
$b = 8.666 \pm 0.002$	
$c = 17.990 \pm 0.001$	
$\beta = 100.521 \pm 0.006^\circ$	
$V = 1197.71 \text{ \AA}^3$	
$\rho_m = 1.56 \text{ g cm}^{-3}$	
$\rho_c = 1.60 \text{ g cm}^{-3}$	$Z = 4$
$\mu(\text{Cu K}\alpha) = 12.2 \text{ cm}^{-1}$	
Space group: $P2_1/c$ (No. 14, C_{2h}^2)	
Crystals: transparent yellow polyhedra	
Biaxial (-)	
$\alpha = 1.528 \pm 0.003$	
$\beta = 1.645 \pm 0.003$	
$\gamma = 1.718 \pm 0.003$	
$x = 1.718 \pm 0.003$	
$x = b$	
$Z \wedge [001] = 74^\circ$	
$2V_\alpha = 67.2^\circ$	

Crystal decay over the course of the experiment, as determined from comparison of the $0kl$ and $0k\bar{l}$ intensities, was 2.8% and linear with X-ray exposure within counting and machine errors. The decreases in intensities of the two most intense check reflections (015 and 140) were 2.5 and 3.1%; changes in the third check reflection were hidden by the large relative error of measurement of this weak reflection.

Lorentz and polarization corrections were applied and corrections for the crystal decay were made in the calculation of the F 's. No absorption corrections were made in view of the low value of μR and the roughly spherical shape of the crystal.

Determination and refinement of the structure

The structure factors were placed on an absolute scale and corrected for thermal motion by least-squares fit to a Wilson (1944) plot, and converted to normalized structure factors. The atomic scattering factors for carbon, nitrogen, and oxygen were taken from *International Tables for X-ray Crystallography* (1962); that for hydrogen was from Stewart, Davidson & Simpson (1965). The statistical distributions of $\langle |E| \rangle$ and $\langle |E^2 - 1| \rangle$ verified that the true space group is centrosymmetric.

A trial structure was obtained using the symbolic addition procedure described by Karle & Karle (1966) with the program *MAGIC* written by Dewar (1968). Table 2 lists the input phases to *MAGIC*. The first three reflections define the origin and were arbitrarily assigned a positive phase, while the remaining starting reflections were given symbolic phases.

The heavy atoms were located in the first E map and the hydrogen atoms were located in the first difference Fourier map. The conventional R index after several cycles of least-squares calculations, in which the hydrogen positions and a secondary extinction parameter (Zachariasen, 1967) were varied in addition to the posi-

tional and anisotropic thermal parameters for the heavy atoms, was 0.043.

Table 2. *Initial symbolic phases used in the application of the \sum_2 relationship*

h	k	l	E	Symbol	Correct phase
3	5	13	4.354	+	+
1	2	$\bar{1}$	3.995	+	+
1	3	0	3.713	+	+
6	5	$\bar{1}\bar{4}$	4.280	B	+
3	7	11	4.125	C	-
5	6	4	3.370	F	+
4	7	$\bar{1}\bar{1}$	3.142	G	+

Refinement after this point was based on F^2 instead of F to allow for the inclusion, with realistic weight, of the reflections with very small or negative net intensities. The quantity minimized in the least squares thus became $\sum w(F_o^2 - F_c^2)^2$.

The weights used were calculated from $w = 1/\sigma^2(F_o^2)$ where

$$\sigma^2(F_o^2) = \frac{1}{S^2 L_p} [C + 2(B_1 + B_2) + (\epsilon_o + PC)^2]. \quad (1)$$

L_p is the Lorentz-polarization correction, S is the scale factor required to put the F 's on an absolute scale, C is the scan count and B_1 and B_2 are backgrounds. The coefficients ϵ_o and P , which presumably reflect machine-dependent errors, were derived from comparisons of multiple measurements of equivalent reflections; these values were 150 and 0.025.

Refinement was then carried out by performing one cycle of full-matrix least squares on all 2377 reflections, varying the scale and extinction parameters and the positional and anisotropic thermal parameters for all the non-hydrogen atoms, and subsequently performing a cycle of full-matrix least squares on the scale, extinction, and hydrogen positional parameters. The hydrogen isotropic B 's were held constant at 3.0. Three tandem least-squares cycles reduced the R' index $\{R' = [\sum w(F_o^2 - F_c^2)^2 / \sum w F_o^2]^{1/2}\}$ from 0.115 to 0.034. Two more tandem cycles were performed in which the parameters of the four carbon atoms to which the hydrogen atoms are bound were included in both matrices and the hydrogen isotropic thermal parameters were also allowed to vary. Refinement was stopped at this point as all the heavy-atom parameter shifts were less than one-half e.s.d. and the shifts in the hydrogen parameters were all less than one e.s.d. During the last four cycles, reflections 043, 131, $22\bar{8}$, $22\bar{2}$, 220, 357, $3\bar{7}9$, $3,10,3$, $43\bar{9}$, and $5,2,1\bar{2}$ were given zero weight; they showed anomalously large residuals, suggesting crystal-setting errors or errors in the recording of the data. The final R' index was 0.027. A final difference Fourier map showed no features above $0.20 \text{ e.}\text{\AA}^{-3}$. Several of the highest peaks on this map were localized between carbon atoms in the picryl group and presumably represent bonding electrons not taken into account by the model. Table 3 lists the final values of the secondary extinction parameter and

the atomic positional and thermal parameters and their errors as determined from the inverse matrix from the final least-squares cycle. The estimated relative standard deviation in the scale factor is 0.12%. The standard deviation of a reflection of unit weight, defined as $\sqrt{\sum w(F_o^2 - F_c^2)/(N - P)}$, where N and P are respectively the number of observations and the number of parameters varied, was 0.72, suggesting that the variances $\sigma^2(F_o^2)$ were overestimated by about 15%. As a check on the validity of the weighting scheme, plots were made of the average value of $|F_o^2 - F_c^2|/\sigma(F_o^2)$ versus the order of data collection, versus intensity and versus $\sin \theta/\lambda$. The first plot was a straight line with zero slope. The second plot indicated a slight intensity dependence, the standard deviations for the weak reflections being slightly high and those for the intense reflections somewhat too low. There is no dependence of the weights upon $\sin \theta/\lambda$ except at very low angles ($\theta < 10^\circ$) where the $\sigma(F^2)$ are too small by about a factor of two. These deviations were not considered to be sufficiently great as to justify the expense of re-refinement with an improved weighting scheme. They do suggest, however, that the value of ϵ_o in equation (1) was too large, perhaps by as much as a factor of two. The observed and calculated structure

factors and the standard deviations in the observed F^2 are given in Table 4.

Description and discussion of the structure

Intramolecular bond distances and angles are given in Fig. 1. Bond distances corrected* and uncorrected for thermal riding motion appear in Table 5. The average estimated error in the angles involving only non-hydrogen atoms is 0.20° and in bond angles involving hydrogen are 1.40° . The true errors in the bond distances and angles may be somewhat larger than those given here since the stated errors are estimated from the inverse matrix of a least-squares refinement in which some of the parameters were held fixed.

The bond distances and angles in the picryl group are normal in comparison with the results of recent three-dimensional structure determinations of nitrobenzene derivatives. Holden & Dickinson (1969) list a large number of such structures. Common structural features of nitrobenzene compounds are the increased internal angles at the carbon atoms to which the nitro

* Corrected bond distances were calculated using a locally modified form of Busing & Levy's program ORFFE (1959) which assumes a single atom riding model.

Table 3. Final least squares parameters and their estimated standard deviations

The standard deviations apply to the rightmost digits of the least-squares parameters. Fractional coordinates are $\times 10^5$ except those for hydrogen, which are $\times 10^4$. The anisotropic thermal parameters have all been multiplied by 10^5 . The anisotropic temperature factor is of the form $\exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$.

The extinction parameter, E , is used to correct F_{calc} to F_{corr} which is then used in the least squares. The extinction correction factor involving E is $F_{\text{corr}} = \text{scale} \times F_{\text{calc}} / (1 + CE)^{1/4}$ where $C = \frac{2(1 + \cos^4 2\theta)F_{\text{calc}}^2}{(1 + \cos^2 2\theta) \sin 2\theta}$.

	x	y	z	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}	$B(\text{\AA}^2)$
C(1)	23216 (22)	50383 (19)	20735 (9)	1426 (33)	864 (26)	257 (6)	37 (24)	185 (12)	25 (10)	
C(2)	7310 (22)	55417 (19)	22366 (9)	1383 (33)	1002 (28)	254 (7)	104 (25)	105 (12)	23 (11)	
C(3)	4598 (22)	58876 (20)	29517 (10)	1429 (35)	1153 (30)	278 (7)	97 (26)	188 (12)	-28 (12)	
C(4)	18388 (24)	56671 (20)	35365 (9)	1755 (39)	984 (27)	240 (6)	-117 (26)	186 (12)	-21 (11)	
C(5)	34430 (23)	51494 (20)	34265 (9)	1480 (34)	1076 (29)	273 (7)	-71 (26)	70 (12)	18 (11)	
C(6)	36651 (22)	48824 (20)	26969 (10)	1316 (33)	1008 (28)	309 (7)	9 (25)	148 (12)	-18 (11)	
C(7)	23545 (40)	60281 (29)	7850 (14)	3425 (71)	1379 (39)	326 (9)	260 (43)	411 (20)	175 (15)	
C(8)	31184 (21)	33032 (21)	11691 (10)	1316 (32)	1246 (30)	297 (7)	27 (26)	149 (12)	-58 (12)	
C(9)	34850 (45)	30584 (36)	3909 (15)	3330 (71)	1789 (48)	335 (9)	671 (51)	445 (21)	-59 (18)	
N(1)	25204 (17)	47391 (15)	13216 (7)	1665 (28)	1025 (22)	249 (5)	148 (21)	222 (9)	20 (9)	
N(2)	-7647 (19)	57186 (20)	16075 (8)	1519 (32)	1562 (31)	285 (6)	254 (26)	163 (10)	23 (11)	
N(3)	16127 (23)	59881 (19)	43173 (9)	2190 (41)	1422 (29)	282 (6)	-45 (28)	228 (13)	-13 (11)	
N(4)	54425 (20)	44564 (20)	26011 (10)	1403 (33)	1612 (31)	404 (7)	-24 (26)	145 (13)	-166 (13)	
O(1)	33257 (15)	23038 (13)	16508 (6)	2095 (27)	1170 (19)	348 (5)	278 (19)	132 (9)	42 (8)	
O(2)	-11804 (17)	46205 (17)	11935 (7)	2010 (29)	2088 (28)	359 (5)	267 (24)	35 (10)	-294 (11)	
O(3)	-14877 (18)	69732 (17)	15459 (7)	2389 (34)	1683 (27)	497 (6)	758 (25)	37 (12)	126 (11)	
O(4)	1747 (20)	63787 (19)	44185 (7)	2452 (35)	2940 (35)	363 (6)	539 (30)	384 (11)	-26 (11)	
O(5)	28815 (19)	58686 (17)	48243 (7)	2487 (35)	2620 (34)	289 (5)	-53 (28)	28 (11)	-106 (11)	
O(6)	62804 (18)	36505 (18)	30845 (9)	1997 (32)	2251 (30)	612 (8)	815 (28)	-15 (12)	62 (13)	
O(7)	59626 (17)	49612 (20)	20513 (8)	1703 (29)	3076 (36)	449 (6)	-286 (27)	369 (11)	-120 (12)	
H(1)	-650 (18)	6239 (17)	3038 (8)							4.28 (36)
H(2)	4400 (17)	4959 (15)	3824 (7)							3.17 (33)
H(3)	3691 (27)	2078 (24)	344 (11)							6.41 (65)
H(4)	4472 (32)	3628 (30)	292 (13)							10.57 (88)
H(5)	2640 (29)	3475 (30)	011 (13)							9.27 (80)
H(6)	3433 (26)	6340 (26)	703 (11)							7.39 (70)
H(7)	1720 (28)	5666 (24)	288 (11)							8.96 (71)
H(8)	1758 (24)	6986 (23)	987 (10)							6.24 (53)

Extinction 0.00159 (7)

groups are attached and O-N-O angles larger than 120°. The internal angle at C(1) is substantially smaller than those at the two unsubstituted carbons, C(3) and

C(5), and the C(1)-C(2) and C(1)-C(6) bond lengths are equal within one standard deviation and are about 0.02 Å longer than the average (1.376 Å) of the other

Table 4. Observed and calculated structure factors and the experimentally estimated standard deviations

Units are electrons. The sign of F_o is the sign of the F_c². Reflections given zero weight in the last least-squares cycle have been assigned σ's of zero. The column headings are k, l, 100F_o, 100F_c, 100F_c, and 10σ(F_c²).

Table with columns: k, l, 100F_o, 100F_c, 100F_c, and 10σ(F_c²). The table contains multiple rows of numerical data representing structure factors and standard deviations for various reflections.

Table 5. Observed bond distances and bond distances corrected for riding motion (Å)

The errors in the least significant digit are given in parentheses.

	Distance	
	Uncorrected	Corrected
C(1)–C(2)	1.398 (3)	
C(2)–C(3)	1.375 (2)	
C(3)–C(4)	1.375 (3)	
C(4)–C(5)	1.379 (3)	
C(5)–C(6)	1.375 (3)	
C(6)–C(1)	1.396 (3)	
C(1)–N(1)	1.413 (2)	1.417 (2)
N(1)–C(7)	1.467 (2)	1.492 (2)
N(1)–C(8)	1.374 (2)	1.374 (2)
C(8)–O(1)	1.215 (2)	1.230 (2)
C(8)–C(9)	1.494 (3)	1.523 (3)
C(2)–N(2)	1.479 (2)	1.486 (2)
N(2)–O(2)	1.216 (2)	1.239 (2)
N(2)–O(3)	1.221 (2)	1.251 (2)
C(4)–N(3)	1.474 (2)	1.484 (2)
N(3)–O(4)	1.218 (2)	1.251 (2)
N(3)–O(5)	1.223 (2)	1.250 (2)
C(6)–N(4)	1.477 (3)	1.490 (3)
N(4)–O(6)	1.210 (2)	1.247 (2)
N(4)–O(7)	1.217 (2)	1.246 (2)
C(3)–H(1)	0.958 (16)	
C(5)–H(2)	0.950 (14)	
C(9)–H(3)	0.872 (23)	
C(9)–H(4)	0.959 (27)	
C(9)–H(5)	0.932 (26)	
C(7)–H(6)	0.922 (23)	
C(7)–H(7)	0.990 (22)	
C(7)–H(8)	1.049 (21)	

four C–C bonds. These results support the hypothesis of Carter, McPhail & Sim (1966) regarding the hy-

bridization of the ring carbon orbitals in substituted aromatics.

The overall conformation of AM246 is very similar to that found by Cady (1967) in the structure determination of *N*-methyl-*N*,2,4,6-tetranitroaniline (tetryl), which differs from AM246 only in that a nitro group replaces the acetyl group.

As in tetryl, the substituent groups in AM246 are rotated out of the plane of the benzene ring by varying amounts. The benzene ring itself is measurably nonplanar, being slightly puckered. The direction cosines (with respect to the real cell axes) of the least-squares plane through the six ring carbon atoms are 0.3035, 0.9478, –0.1514 and the origin-to-plane distance is 4.128 Å. The r.m.s. deviation of these six atoms from the plane is 0.013 Å, or roughly six times the average standard deviation in their positional parameters. Fig. 2 gives the deviations of these and other atoms from this plane.

The distortion from planarity may be visualized most easily by considering the carbon atoms and the substituent nitro groups at the 2 and 6 positions as being twisted slightly above and below, respectively, the plane of the other four carbon atoms ('up' being here defined as the direction toward the *N*-acetyl oxygen). Atom N(4) shows an additional displacement below the plane, leading to significantly nonplanar bonding about C(6). This distortion surely results from the overcrowding of the three substituents at this end of the molecule, and is small compared with that observed in some other overcrowded aromatic nitro

Table 6. Conformers of anilides

The conformation of the more stable conformer is given. Equilibrium conformer ratios are generally very strongly solvent dependent and are not reproduced here although this information is contained in most of the references cited.

The minimum angle in degrees between the amide and benzene planes found in the model building experiment is given in parentheses as (*endo/exo*).

The specific steric interaction which determines the conformation is given as the type '1a', '1b', or '2' as described in the text. A '3' indicates that inductive-electrostatic effects predominate.

	–H	–CH ₃	<i>N</i> -Substituent –C ₂ H ₅	– <i>n</i> -butyl	– <i>s</i> -butyl	– <i>t</i> -butyl
Formanilide	<i>exo</i> + <i>endo</i> ^{a,b,c} (marked solvent effects)	<i>exo</i> ^g (45/45)	<i>exo</i> ^g (45/45)			<i>endo</i> ^b (2) (70/70)
Acetanilide	<i>endo</i> ^{a,d,e,f} (1a) (35/60)	<i>exo</i> ^{e,g} (2) (45/60)	<i>exo</i> ^{e,g} (2) (45/60)	<i>exo</i> ^e (2) (60/60)	<i>exo</i> ^e (2) (70/70)	<i>exo</i> ^e (2) (70/70)
2,6-Diiodo- acetanilide	<i>endo</i> ^h (1a) (60/75)	<i>exo</i> ^h (2) (75/75)				
2,6 and 2,4,6- Trialkyl- acetanilide	<i>endo</i> ^{l,m} (1a) (60/60) alkyl = Me to (90/90) alkyl = <i>t</i> -Bu	<i>exo</i> ^m (1b) (70/70) Me to (90/90) <i>t</i> -Bu				
2,6 and 2,4,6- Trinitro- acetanilide	<i>endo</i> ^j (1a) (55/75)	<i>endo</i> ^{j,k} (3) (65/85)	<i>endo</i> ^j (3) (65/85)	<i>endo</i> ^j (3) (65/85)	<i>exo</i> ^j (2) (90/90)	<i>exo</i> ^j (2) (90/90)

- a. Russell & Thompson (1956).
 b. Sidall & Stewart (1967).
 c. Hallam & Jones (1970).
 d. Brown & Corbridge (1954).
 Brown (1966).
 e. Carter (1967).
 f. Dyal & Kemp (1966).
 g. Bourn, Gillies & Randall (1966).

- h. Pedersen & Pedersen (1965).
 Pedersen (1967).
 i. Kessler & Rieker (1967).
 j. Weil, Blum, Heiss & Kinnaird (1967).
 k. This work.
 l. Fischer (1968).
 m. Brown, Radom, Sternhill & Rae (1968).

compounds (Akopyan, Kitaigorodsky & Struchkov, 1965). In order to accommodate the amide group and its substituents, the nitro groups at the 2 and 6 positions are rotated 54 and 36° respectively from the plane of the benzene ring. The nitro group at the 4 position, which is not overcrowded, is rotated by only 4° out of the plane of the ring. All of these rotations have the same sense as viewed from the exterior of the molecule.

In spite of the different torsional angles of the nitro groups relative to the benzene plane, the C–N distances at the nitro groups in AM246 are equal within the accuracy of measurement. The average of the three values, 1.487 Å (corrected for thermal motion), is in excellent agreement with the single bond value of 1.49 Å for nitromethane and is also in good agree-

ment with the average of 1.48 Å found for a number of nitro aromatic hydrocarbons (Trotter, 1960), most of them having high torsional angles about the C–N bond. The independence of the C–N bond length and the torsion angle about the C–N bond is in agreement with the conclusions of Carter *et al.* (1966) and Holden & Dickinson (1969). The average of the six corrected N–O distances is 1.247 Å, in good agreement with reported values for similar molecules.

The C(1)–N(1) bond is 1.417 (2) Å long, in excellent agreement with the corresponding bond in tetryl [1.419 (4) Å; Cady, 1970]. The torsion angle about this bond is very nearly the same in the two compounds and π overlap would be expected to be somewhat less than 25% ($\cos^2 60^\circ$) of maximum. Both of these

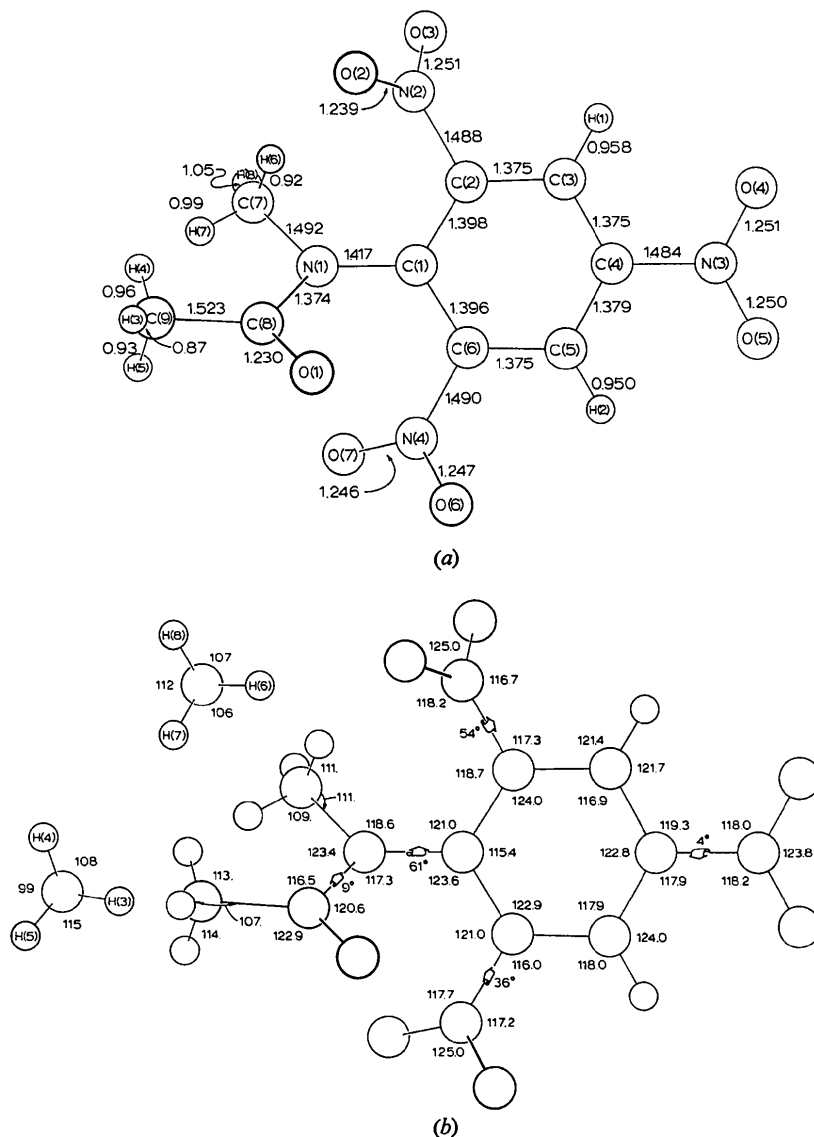


Fig. 1. (a) Bond distances (Å) and (b) angles (°) in *N*-methyl-2,4,6-trinitroacetanilide. The angular deviations from planarity about the various C–N bonds and the senses of these deviations are indicated. The methyl groups are also shown in projection for clarity.

distances are substantially shorter than the 1.470 (5) Å proposed by Camerman (1970) for the length of a $C(sp^2)-N(sp^2)$ single bond. In *N*-methylacetanilide, in which the amide group lies in a mirror plane perpendicular to the benzene ring, the $C(\text{aryl})-N(\text{amide})$ bond distance was found to be 1.481 Å (Pedersen, 1967), consistent with the complete lack of π character in this bond. It is curious that the bond lengths for this C–N bond in AM246 and tetryl are both close to the value of 1.413 Å found for the same bond in the structure of acetanilide (Brown, 1966) where the acetamide plane makes an angle of only 17.6° with the plane of the benzene ring. Since the major difference between the three compounds is the three nitro groups possessed by AM246 and tetryl, one would expect, by simple resonance structure arguments, that the C–N bond would be weaker, and consequently longer, in the trinitro derivatives than in acetanilide itself, particularly in view of the increased torsion angle. Gramaccioli, Destro & Simonetta (1968) have found a similarly puzzling short bond between the C(1) carbon and the ethoxy oxygen in 2,4,6-trinitrophenetole. Simple coulomb attraction between opposite charges

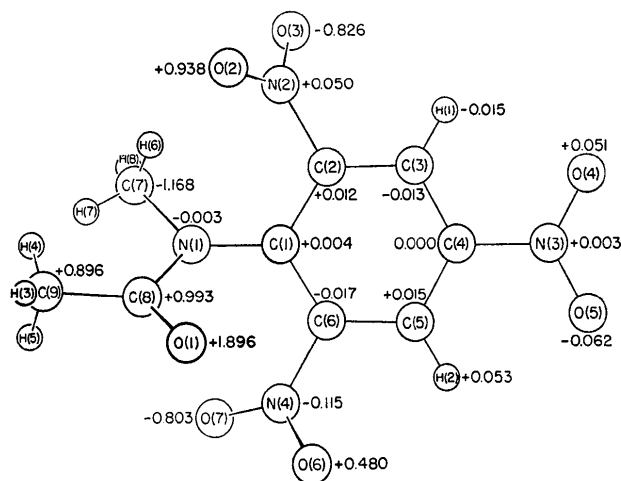


Fig. 2. Deviations (Å) from the least-squares plane through the benzene carbons.

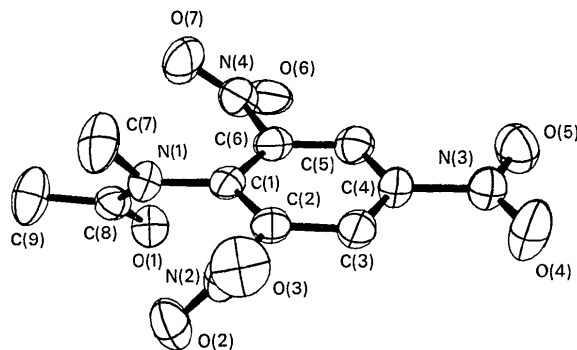


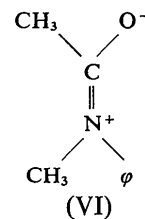
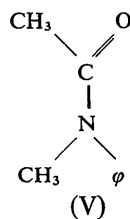
Fig. 3. Thermal motion of the molecule. Thermal ellipsoids are drawn at the 50% probability level.

on C(1) and N(1) induced by the acetyl and the nitro groups could account for this shortening.

The acetyl group attached to N(1) is in the *endo* conformation, in agreement with the n.m.r. results of Weil *et al.* (1967). The acetamide group is significantly nonplanar; the acetyl moiety is twisted about 9° relative to the plane C(7)–N(1)–C(8) because of interaction between O(1) and N(4) (2.85 Å, a normal van der Waals contact) and the C(7) methyl group is bent away from N(2) (3.08 Å, a relatively short van der Waals contact). The least-squares plane containing N(1), C(1), C(7) and C(8) makes a dihedral angle of 60° with the least-squares plane of the six ring carbons. This C–N torsion angle has the same sense as that of the *ortho* nitro groups.

The amido group is sterically forbidden from making an angle of less than 60° with respect to the plane of the benzene ring. In solution, it is likely that the amido moiety torsionally oscillates about the C(1)–N(1) bond between the nitro group 'stops', with an average dihedral angle of 90° relative to the benzene ring. The fact that we observe the amide group resting against one of the stops does not preclude, but rather supports the assumption of Weil *et al.* (1967) that the amide group is, on the average, perpendicular to the benzene ring.

In spite of the distortions resulting from the steric interactions, the distances and angles in the amido group are very similar to those found in related compounds and in the peptide linkage. The C(8)–N(1)



bond possesses considerable π character; however, it is slightly longer than the 1.34₃ Å found for this bond in formamide (Kurland & Wilson, 1957) and *N*-methylacetanilide, while C(8)–O(1) is slightly shorter than the C–O distances (1.23 and 1.263 Å) in these two molecules. This indicates that resonance form (VI) does not contribute as much and form (V) contributes correspondingly more to the structure of the AM246 amide group than in the other two molecules. The C(8)–C(9) and N(1)–C(7) distances are both reasonable and compare well with Pauling's (1960) average values for those in a typical peptide linkage.

Views of this structure are shown in Fig. 4. There are two intermolecular distances that are slightly shorter than normal van der Waals contacts. The first of these contacts is between H'(8), a methyl hydrogen, and O(6), a nitro group oxygen. The H'–O and C'–O distances are 2.41 and 3.10 Å, the C'–H'–O and H'–O–N angles are 121 and 176° respectively. Although the H'–O distance is nearly 0.2 Å shorter than the

expected 2.6 Å van der Waals contact, the geometry of the situation, plus the fact that H'(8) is a methyl hydrogen indicates that this is probably not a hydrogen bond but simply a short contact.

The second contact, between H'(1), one of the picryl

hydrogens, and O(1), the carbonyl oxygen, is 2.43 Å long. Here the geometry is more favorable; the C'(3)-O(1) distance is 3.40 Å and the C'(3)-H'(1)-O(1) and H'(1)-O(1)-C(8) angles are 174 and 115° respectively. Since the hydrogen atom H'(1) resides on a

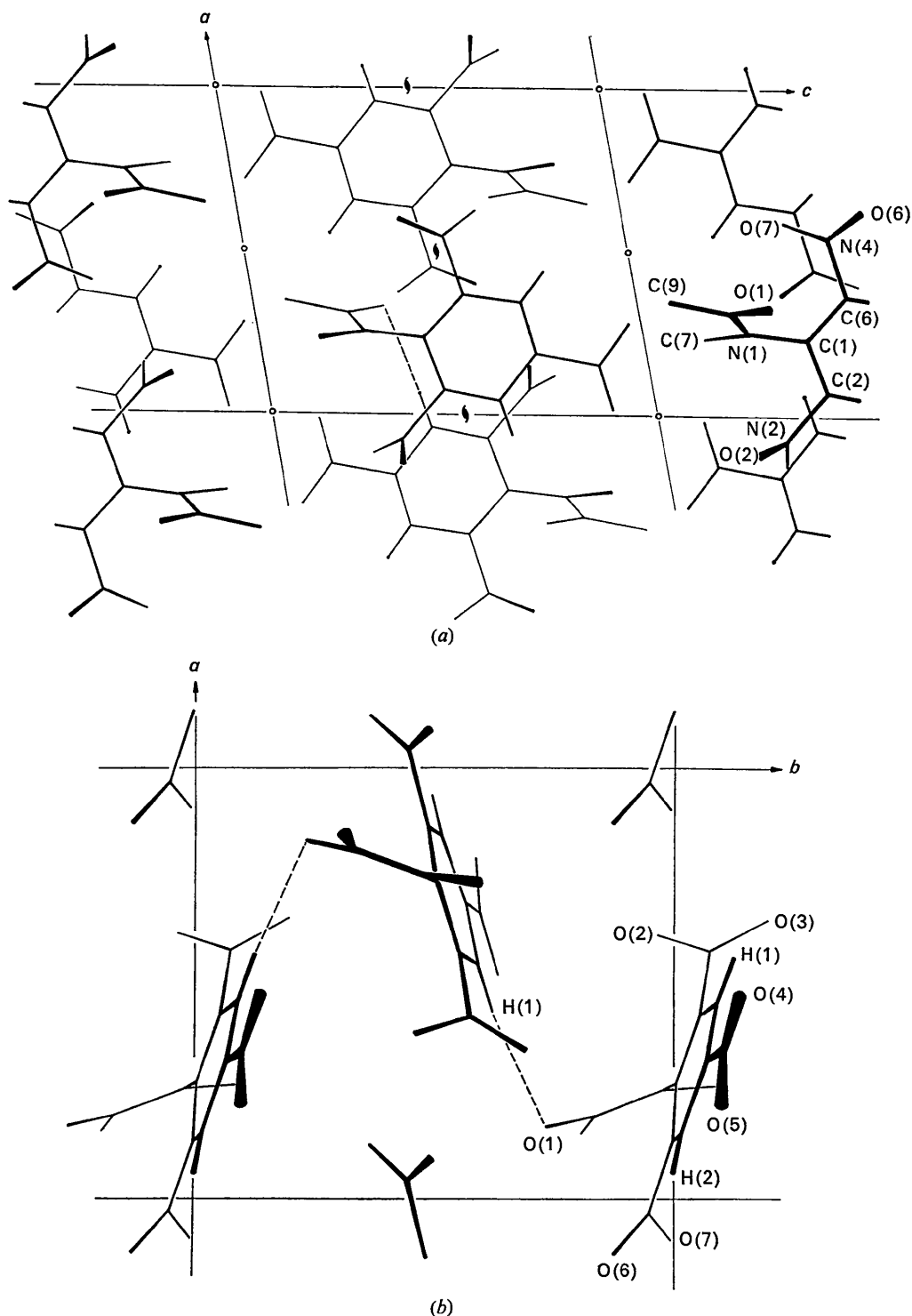


Fig. 4. Projection of the cell contents (a) down the *b* axis and (b) down the *c* axis.

carbon atom rendered somewhat positive by the inductive effects of the nitro groups, this hydrogen atom may be more capable of participating in a hydrogen bond than if it were, for example, an ordinary methyl hydrogen. Also, we expect O(1), because of the considerable contribution of resonance form (VI) which places an extra electron on it, to be an excellent hydrogen-bond acceptor. Cady (1967) found a very similar 'weak' hydrogen bond involving a picryl hydrogen in the structure of tetryl and has noted the existence of several others in other polynitro aromatics.

The thermal motions are best understood by looking at Fig. 3. The largest excursions are predictably those of the nitrate oxygens and of the two methyl groups, and are all in directions perpendicular to the bonds linking them to the rest of the molecule.

Discussion of conformation of anilides

Although the overall conformation of a molecule is the consequence of the net effect of all the forces and interactions to which it is subject, it is generally sufficient to consider steric forces alone in predicting conformational stabilities. It is thus often very useful to construct space-filling models in order to evaluate the magnitudes of the steric interactions, particularly when there are several competing effects which can influence the conformation, as in the substituted and unsubstituted acetanilides and formanilides. Table 6 summarizes the conformational results of crystallographic, infrared and n.m.r. investigations on a variety of acetanilides and formanilides as well as the results of model-building experiments using CPK space-filling models.

With the exception of the *ortho*-substituted acetanilides, in which the inductive effects of the substituents are very important, the stable conformers of these compounds can all be predicted using a single steric rule and the assumption that the aryl and amide moieties will tend towards coplanarity in order to

maximize their π -overlap. The only steric requirement is that the two bulkiest groups be *trans* across the C(acetyl)-N(amide) bond.

Only two specific types of steric interactions are involved: (1) interactions between the *ortho* hydrogens or *ortho* substituents and (a) the acetyl group or (b) the *N*-alkyl substituent; (2) interactions between the acetyl methyl group and the *N*-alkyl substituent. The second appears to be a somewhat stronger interaction than the first and can overcome the tendency towards coplanarity of the amide and benzene.

Acetanilide and *N*-methylacetanilide are two representative samples:

Acetanilide

The *endo* conformation permits the amide group to be more nearly coplanar with the benzene ring, since the acetyl oxygen with a van der Waals radius of 1.4 Å permits a closer approach to the *ortho* hydrogen than does the acetyl methyl (2.0 Å) in the *exo* conformation. For a lone molecule in an apolar medium there are no other significant interactions.

N-Methylacetanilide

N-Methylation reverses the stabilities of the acetanilide conformers. In the *endo* conformer the acetyl methyl and *N*-methyl groups interact with one another; in the *exo* conformer this strain is relieved at the expense of interaction between the benzene ring and the acetyl methyl group. This latter interaction, however, is minimized when the amide plane is perpendicular to the benzene ring. Thus the *exo* conformer is the more stable, in spite of the loss of resonance energy.

It is apparent from the results of this structural investigation that in the substituted acetanilides inductive and electrostatic effects must be taken into account in order to predict the more stable conformer. Knowledge of the atomic charge densities would be of obvious value; however, these are not available for the range of molecules involved here. Fig. 5 gives the atomic charge densities for acetanilide recently calculated at the CNDO/2 level of approximation (Olsen & Kang, 1970). Although it may be argued that the values from such calculation are inexact, they may serve as a starting point for the qualitative arguments below. The calculated distance between C(1) and the acetyl oxygen for the geometry pictured is about 2.75 Å; for AM246 this distance is 2.65 Å. The distance of either of the two *ortho* carbons to the oxygen is approximately 3.3 Å. The simple electrostatic attraction between the oxygen and C(1) is consequently an important source of stabilization energy for the *endo* conformer. The charge densities shown change only slightly if the *exo* geometry is used or if the amide plane is assumed to be coplanar with the benzene ring for the *endo* conformer.

Calculations for the trinitroacetanilides have not been carried out; however, the effect of three nitro

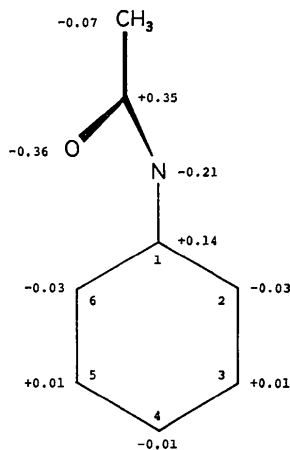


Fig. 5. Charge densities in acetanilide. The amide plane is taken to be perpendicular to the benzene ring.

substituents on the charge densities of the benzene ring can be qualitatively predicted. The inductive effect of a nitro group is to stabilize negative charge at the atom to which it is attached. Nitro groups at the 2, 4, and 6 positions consequently enhance the effect of the acetamide group and result in a greater concentration of positive charge at C(1) than for the unsubstituted acetanilide. Thus, the *endo* conformer, which places O(1) over C(1), is substantially stabilized even if type 2 steric interactions are present. The observed conformers for the series of *N*-substituted trinitroacetanilides support this argument. The *endo* conformer is stabilized for *n*-alkyl substituents, as found here for AM246, and the *exo* conformer is assumed only when the *N*-substituents are bulky secondary or tertiary alkyl groups.

The trend of decreasing relative stability for the *endo* conformer in the 2,6- dialkyl and 2,4,6-trialkyl substituted acetanilides for the series alkyl=methyl, ethyl, isopropyl, *t*-butyl, is also in agreement with the above arguments. The equilibrium ratios of *endo* to *exo* conformers for this series are 2·8, 2·2, 1·7, 1·2 (Kessler & Rieker, 1967). Since the stabilizing power of alkyl groups for positive charges increases in the order primary, secondary, tertiary, the positive charge at C(1) can be expected to be increasingly destabilized and consequently the *exo* conformer increasingly stabilized relative to the *endo* conformer.

An interesting test of this argument would be the examination of the equilibrium conformer ratio for 2,4,6-trifluoroacetanilide. The value to be expected for the *endo-exo* ratio is less than unity; the *exo* conformer should predominate both in solution and in the solid.

The steric and inductive-electrostatic arguments given above can be expected to be equally valid for the thioacetanilides and thioformanilides which have also been extensively studied (Walter & Huehnerfuss, 1969; Rae, 1967; Jones & Smith, 1968; Hallam & Jones, 1970).

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