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N-(4-Ethoxy-2,5-dinitrophenyl)acetamide

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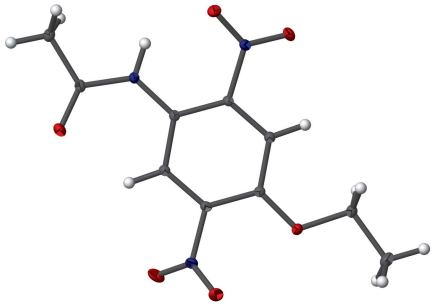
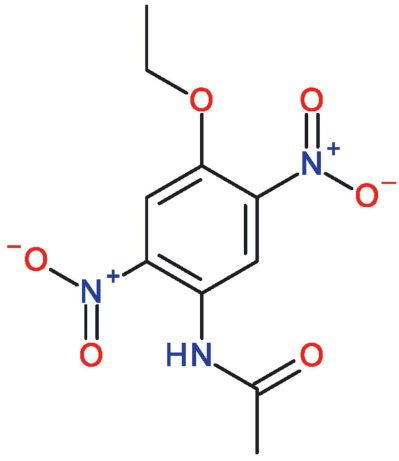
In the title compound, $C_{10}H_{11}N_3O_6$, the torsion angles about the bonds to the benzene ring are less than 4°, except for the nitro groups, which are twisted out of the ring plane by 25.27 (3) and 43.63 (2)°. The N—H group forms a bifurcated hydrogen bond, with an intramolecular component to a nitro group O atom and an intermolecular component to the other nitro group, thereby forming chains propagating in the [010] direction. Several weak C—H···O interactions are also present.

3D view



Chemical scheme



Structure description

The analgesic use of 4-acetamidophenetole (4-AcP) predates the First World War. 4-AcP was likely the first synthetic chemical to go on the market as a fever reducer, but was withdrawn from global markets three decades ago due to its carcinogenic and kidney-damaging properties (Zeman, 1963; Carrociampi, 1978; Leistenschneider *et al.*, 1983; Holmäng *et al.*, 2013). However, in view of 4-AcP's physical appearance and textural similarities to cocaine, in recent years, there have been several instances of 4-AcP being used as an adulterant or cutting agent (Broséus *et al.*, 2016). Thus, phenacetin is still in use, however, now in the form of an illicit drug. We believe that 4-AcP, like its putative major metabolite, 4-acetamidophenol (4-AP) (Hinson, 1983; Lakshmi *et al.*, 2000; Liu *et al.*, 2019), undergoes oxidative transformation by cellular oxidants such as hypochlorite/hypochlorous acid and peroxynitrite/peroxynitrous acid and forms chlorinated and nitrated products. Towards understanding this and to shed light on molecular targets, we have synthesized the title compound 2,5-dinitro-4-AcP, $C_{10}H_{11}N_3O_6$, and we now report its structure. The results of the present study, together with the recent understanding of the mechanisms of action of 4-acetamidophenol (4-AP), which proceeds through hydrolysis and subsequent formation of arachidonic acid conjugates and their binding

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2N···O3	0.900 (10)	2.015 (10)	2.6875 (6)	130.5 (8)
N2—H2N···O6^{i}	0.900 (10)	2.618 (10)	3.4308 (6)	150.5 (8)
C5—H5A···O4	0.95	2.20	2.8386 (7)	123
C8—H8A···O2^{ii}	0.98	2.63	3.3768 (9)	133
C10—H10A···O2^{iii}	0.98	2.37	3.3367 (7)	171
C10—H10B···O5^{i}	0.98	2.65	3.5677 (8)	155

Symmetry codes: (i) $x, y+1, z$; (ii) $x, y-1, z$; (iii) $x, y, z+1$.

cannabinoid receptors, may be useful in providing insights into molecular targets for 4-AcP and its metabolites.

The ethoxy group is nearly coplanar with the phenyl ring, having a C2—C1—O1—C7 torsion angle of 1.43 (8)° and C1—O1—C7—C8(Me) torsion angle of 174.56 (5)°, as shown in Fig. 1. The acetamido group is also nearly coplanar with the phenyl ring, having a C5—C4—N2—C9 torsion angle of 3.18 (9)°. The N1/O2/O3 nitro group adjacent to the acetamido substituent is twisted out of the phenyl plane by 25.27 (3)°, and the N3/O5/O6 group adjacent to the ethoxy group forms a dihedral angle of 43.63 (2)° with respect to the C1–C6 ring.

The N2—H2N group forms a bifurcated hydrogen bond (Table 1), with an intramolecular component to the adjacent nitro group [N2···O3 = 2.6875 (6) Å] and a longer intermolecular component to the other nitro group [N2···O6^{i} = 3.4308 (6) Å; symmetry code: (i) $x, y+1, z$], forming chains propagating in the [010] direction, as shown in Fig. 2. Several C—H···O interactions are also present (Table 1), which together with the N—H···O hydrogen bond lead to (100) sheets.

Synthesis and crystallization

2,5-Dinitro-4-AcP was synthesized by nitration of 4-AcP using nitric acid–sulfuric acid mixtures (0–5°C) and subsequent purification by column chromatography on alumina or silica gel as described by Russell *et al.* (1990). Yellow needles were grown by slow evaporation from methanol solution.

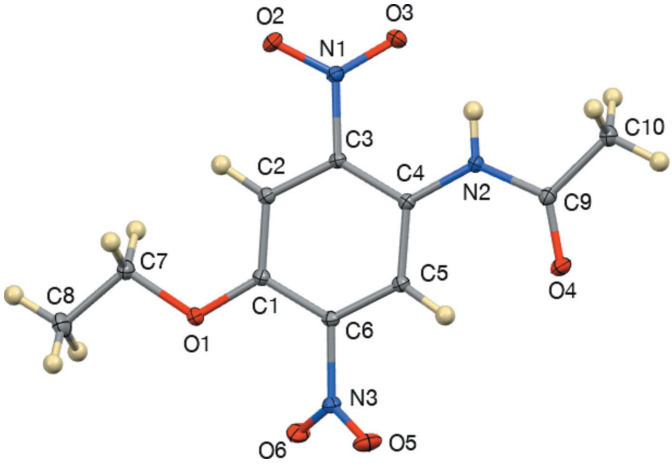


Figure 1
The title molecule showing 50% displacement ellipsoids.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{10}H_{11}N_3O_6$
M_r	269.22
Crystal system, space group	Triclinic, $P\overline{1}$
Temperature (K)	90
a, b, c (Å)	6.7463 (3), 9.0360 (4), 9.3954 (4)
α, β, γ (°)	81.005 (2), 85.099 (2), 88.700 (2)
V (Å^3)	563.60 (4)
Z	2
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.13
Crystal size (mm)	0.30 × 0.10 × 0.09
Data collection	
Diffractometer	Bruker Kappa APEXII DUO CCD
Absorption correction	Multi-scan (*SADABS*; Krause *et al.*, 2015)
T_{min}, T_{max}	0.920, 0.988
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	29518, 7110, 5824
R_{int}	0.043
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.911
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.038, 0.111, 1.04
No. of reflections	7110
No. of parameters	177
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.76, −0.28

Computer programs: *APEX3* and *SAINT* (Bruker, 2016), *SHELXS97* (Sheldrick, 2008), *SHELXL2017/1* (Sheldrick, 2015), *Mercury* (Macrae *et al.*, 2020) and *publCIF* (Westrip, 2010).

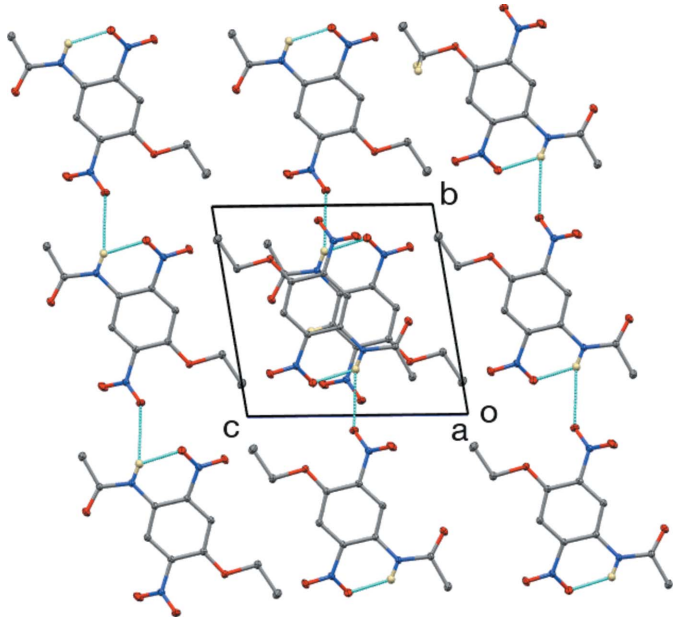


Figure 2
The unit cell viewed down [100], showing hydrogen bonds as blue lines. C—H hydrogen atoms are not shown.

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2.

Funding information

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full crystallographic data

IUCrData (2020). **5**, x201121 [https://doi.org/10.1107/S2414314620011219]

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Crystal data

$C_{10}H_{11}N_3O_6$
$M_r = 269.22$
Triclinic, $P\overline{1}$
$a = 6.7463$ (3) Å
$b = 9.0360$ (4) Å
$c = 9.3954$ (4) Å
$\alpha = 81.005$ (2)°
$\beta = 85.099$ (2)°
$\gamma = 88.700$ (2)°
$V = 563.60$ (4) Å^3
$Z = 2$
$F(000) = 280$
$D_x = 1.586$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 9965 reflections
$\theta = 3.0$–$40.2°$
$\mu = 0.13$ mm^{-1}
$T = 90$ K
Needle, yellow
0.30 × 0.10 × 0.09 mm

Data collection

Bruker Kappa APEXII DUO CCD diffractometer
Radiation source: fine-focus sealed tube
TRIUMPH curved graphite monochromator
φ and ω scans
Absorption correction: multi-scan (SADABS; Krause *et al.*, 2015)
$T_{min} = 0.920$, $T_{max} = 0.988$
29518 measured reflections
7110 independent reflections
5824 reflections with $I > 2\sigma(I)$
$R_{int} = 0.043$
$\theta_{max} = 40.4°$, $\theta_{min} = 2.2°$
$h = -11 \rightarrow 12$
$k = -15 \rightarrow 16$
$l = -17 \rightarrow 15$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.038$
$wR(F^2) = 0.111$
$S = 1.04$
7110 reflections
177 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Hydrogen site location: mixed
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0597P)^2 + 0.0585P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.76$ e Å^{-3}
$\Delta\rho_{min} = -0.28$ e Å^{-3}

Special details

Geometry. All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Refinement. All H atoms were located in difference maps and those on C were thereafter treated as riding in geometrically idealized positions with C—H distances 0.95 Å for phenyl, 0.99 Å for CH_2 and 0.98 Å for methyl. Coordinates of the N—H hydrogen atom were refined. U_{iso}(H) values were assigned as $1.2U_{eq}$ for the attached C or N atom (1.5 for methyl).

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.69178 (7)	0.25306 (4)	0.22213 (4)	0.01208 (7)
O2	0.80562 (9)	0.79863 (5)	0.13502 (5)	0.02166 (10)
O3	0.94649 (7)	0.84282 (5)	0.32212 (5)	0.01549 (8)
O4	0.74286 (8)	0.55569 (5)	0.80156 (5)	0.01579 (8)
O5	0.54980 (7)	0.15057 (5)	0.63040 (5)	0.01655 (9)
O6	0.76371 (8)	0.07153 (5)	0.47211 (5)	0.01675 (9)
N1	0.84988 (7)	0.76273 (5)	0.25917 (5)	0.01119 (8)
N2	0.78930 (7)	0.69046 (5)	0.57358 (5)	0.01020 (7)
H2N	0.8235 (15)	0.7816 (11)	0.5253 (10)	0.012*
N3	0.66942 (7)	0.17087 (5)	0.52301 (5)	0.01052 (7)
C1	0.72020 (8)	0.36104 (5)	0.30173 (5)	0.00923 (8)
C2	0.76108 (8)	0.50980 (6)	0.24458 (5)	0.00986 (8)
H2A	0.768693	0.540555	0.142853	0.012*
C3	0.79085 (8)	0.61374 (5)	0.33497 (5)	0.00893 (8)
C4	0.77060 (7)	0.58036 (5)	0.48682 (5)	0.00857 (8)
C5	0.72406 (7)	0.43112 (5)	0.54384 (5)	0.00912 (8)
H5A	0.705143	0.401790	0.645627	0.011*
C6	0.70546 (7)	0.32621 (5)	0.45315 (5)	0.00893 (8)
C7	0.71005 (9)	0.29652 (6)	0.06650 (6)	0.01309 (9)
H7A	0.840288	0.344280	0.034497	0.016*
H7B	0.603451	0.368885	0.036447	0.016*
C8	0.69258 (11)	0.15636 (7)	0.00051 (7)	0.01860 (11)
H8A	0.799779	0.086200	0.030043	0.028*
H8B	0.702903	0.181958	−0.105121	0.028*
H8C	0.563670	0.109681	0.033650	0.028*
C9	0.77619 (8)	0.67490 (6)	0.72252 (5)	0.01021 (8)
C10	0.80679 (9)	0.81975 (6)	0.77720 (6)	0.01351 (9)
H10A	0.805013	0.800989	0.882891	0.020*
H10B	0.699950	0.890571	0.748418	0.020*
H10C	0.935357	0.862121	0.735925	0.020*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.01876 (18)	0.00903 (15)	0.00891 (14)	−0.00178 (12)	−0.00191 (12)	−0.00211 (11)
O2	0.0418 (3)	0.01400 (18)	0.00889 (16)	−0.00649 (18)	−0.00647 (17)	0.00250 (13)
O3	0.0220 (2)	0.01191 (16)	0.01286 (16)	−0.00698 (14)	−0.00066 (14)	−0.00239 (13)
O4	0.0251 (2)	0.01173 (16)	0.00957 (15)	−0.00162 (14)	−0.00047 (14)	0.00104 (12)
O5	0.01628 (19)	0.01397 (17)	0.01650 (18)	−0.00063 (14)	0.00464 (14)	0.00348 (14)
O6	0.0270 (2)	0.00892 (16)	0.01395 (17)	0.00363 (14)	0.00026 (15)	−0.00213 (13)

N1	0.01583 (19)	0.00887 (16)	0.00837 (15)	−0.00144 (13)	0.00098 (13)	−0.00063 (12)
N2	0.01441 (18)	0.00899 (16)	0.00720 (15)	−0.00176 (13)	−0.00061 (13)	−0.00115 (12)
N3	0.01234 (18)	0.00852 (16)	0.01048 (16)	−0.00062 (13)	−0.00219 (13)	−0.00006 (12)
C1	0.01055 (18)	0.00821 (17)	0.00896 (17)	−0.00029 (13)	−0.00101 (13)	−0.00125 (13)
C2	0.01238 (19)	0.00864 (17)	0.00846 (17)	−0.00046 (14)	−0.00077 (14)	−0.00106 (13)
C3	0.01064 (18)	0.00772 (16)	0.00810 (16)	−0.00083 (13)	−0.00041 (13)	−0.00031 (13)
C4	0.00907 (17)	0.00864 (17)	0.00797 (16)	−0.00039 (13)	−0.00065 (13)	−0.00115 (13)
C5	0.01008 (18)	0.00848 (17)	0.00854 (17)	−0.00012 (13)	−0.00084 (13)	−0.00044 (13)
C6	0.00947 (18)	0.00756 (17)	0.00939 (17)	−0.00010 (13)	−0.00098 (13)	−0.00012 (13)
C7	0.0193 (2)	0.01123 (19)	0.00900 (18)	−0.00058 (16)	−0.00162 (16)	−0.00213 (14)
C8	0.0270 (3)	0.0157 (2)	0.0145 (2)	−0.0029 (2)	−0.0004 (2)	−0.00697 (18)
C9	0.01131 (19)	0.01111 (18)	0.00811 (17)	0.00027 (14)	−0.00081 (13)	−0.00121 (14)
C10	0.0185 (2)	0.0127 (2)	0.00990 (18)	−0.00142 (16)	−0.00154 (16)	−0.00304 (15)

Geometric parameters (Å, º)

O1—C1	1.3451 (6)	C2—H2A	0.9500
O1—C7	1.4489 (7)	C3—C4	1.4068 (7)
O2—N1	1.2214 (6)	C4—C5	1.4031 (7)
O3—N1	1.2327 (6)	C5—C6	1.3845 (7)
O4—C9	1.2225 (7)	C5—H5A	0.9500
O5—N3	1.2299 (6)	C7—C8	1.5058 (8)
O6—N3	1.2228 (6)	C7—H7A	0.9900
N1—C3	1.4677 (7)	C7—H7B	0.9900
N2—C9	1.3798 (7)	C8—H8A	0.9800
N2—C4	1.3953 (6)	C8—H8B	0.9800
N2—H2N	0.900 (10)	C8—H8C	0.9800
N3—C6	1.4698 (7)	C9—C10	1.5035 (8)
C1—C2	1.3918 (7)	C10—H10A	0.9800
C1—C6	1.4036 (7)	C10—H10B	0.9800
C2—C3	1.3895 (7)	C10—H10C	0.9800
C1—O1—C7	116.70 (4)	C5—C6—C1	123.59 (4)
O2—N1—O3	123.54 (5)	C5—C6—N3	116.61 (4)
O2—N1—C3	117.91 (5)	C1—C6—N3	119.79 (4)
O3—N1—C3	118.51 (4)	O1—C7—C8	107.33 (4)
C9—N2—C4	128.40 (4)	O1—C7—H7A	110.2
C9—N2—H2N	116.4 (6)	C8—C7—H7A	110.2
C4—N2—H2N	115.0 (6)	O1—C7—H7B	110.2
O6—N3—O5	124.77 (5)	C8—C7—H7B	110.2
O6—N3—C6	117.66 (4)	H7A—C7—H7B	108.5
O5—N3—C6	117.55 (4)	C7—C8—H8A	109.5
O1—C1—C2	124.44 (5)	C7—C8—H8B	109.5
O1—C1—C6	119.56 (4)	H8A—C8—H8B	109.5
C2—C1—C6	115.99 (4)	C7—C8—H8C	109.5
C3—C2—C1	120.59 (4)	H8A—C8—H8C	109.5
C3—C2—H2A	119.7	H8B—C8—H8C	109.5
C1—C2—H2A	119.7	O4—C9—N2	123.41 (5)

C2—C3—C4	123.56 (4)	O4—C9—C10	123.63 (5)
C2—C3—N1	114.48 (4)	N2—C9—C10	112.96 (4)
C4—C3—N1	121.95 (4)	C9—C10—H10A	109.5
N2—C4—C5	122.78 (4)	C9—C10—H10B	109.5
N2—C4—C3	121.68 (4)	H10A—C10—H10B	109.5
C5—C4—C3	115.50 (4)	C9—C10—H10C	109.5
C6—C5—C4	120.61 (4)	H10A—C10—H10C	109.5
C6—C5—H5A	119.7	H10B—C10—H10C	109.5
C4—C5—H5A	119.7		

C7—O1—C1—C2	1.43 (8)	N2—C4—C5—C6	179.44 (5)
C7—O1—C1—C6	−179.73 (5)	C3—C4—C5—C6	1.54 (7)
O1—C1—C2—C3	−179.20 (5)	C4—C5—C6—C1	−3.56 (8)
C6—C1—C2—C3	1.92 (8)	C4—C5—C6—N3	176.11 (5)
C1—C2—C3—C4	−3.97 (8)	O1—C1—C6—C5	−177.20 (5)
C1—C2—C3—N1	174.85 (5)	C2—C1—C6—C5	1.74 (8)
O2—N1—C3—C2	23.69 (7)	O1—C1—C6—N3	3.14 (7)
O3—N1—C3—C2	−154.05 (5)	C2—C1—C6—N3	−177.92 (5)
O2—N1—C3—C4	−157.47 (6)	O6—N3—C6—C5	−136.01 (5)
O3—N1—C3—C4	24.79 (8)	O5—N3—C6—C5	42.40 (7)
C9—N2—C4—C5	3.18 (9)	O6—N3—C6—C1	43.67 (7)
C9—N2—C4—C3	−179.04 (5)	O5—N3—C6—C1	−137.92 (5)
C2—C3—C4—N2	−175.80 (5)	C1—O1—C7—C8	174.56 (5)
N1—C3—C4—N2	5.47 (8)	C4—N2—C9—O4	−0.69 (9)
C2—C3—C4—C5	2.13 (8)	C4—N2—C9—C10	179.41 (5)
N1—C3—C4—C5	−176.60 (5)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N2—H2*N*···O3	0.900 (10)	2.015 (10)	2.6875 (6)	130.5 (8)
N2—H2*N*···O6^{i}	0.900 (10)	2.618 (10)	3.4308 (6)	150.5 (8)
C5—H5*A*···O4	0.95	2.20	2.8386 (7)	123
C8—H8*A*···O2^{ii}	0.98	2.63	3.3768 (9)	133
C10—H10*A*···O2^{iii}	0.98	2.37	3.3367 (7)	171
C10—H10*B*···O5^{i}	0.98	2.65	3.5677 (8)	155

Symmetry codes: (i) *x*, *y*+1, *z*; (ii) *x*, *y*−1, *z*; (iii) *x*, *y*, *z*+1.