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N-[4-(2-Propyn-1-yloxy)phenyl]-acetamide

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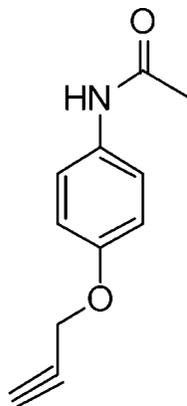
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Key indicators: single-crystal X-ray study; $T = 100$ K; mean $\sigma(\text{C}-\text{C}) = 0.002$ Å; R factor = 0.037; wR factor = 0.100; data-to-parameter ratio = 18.2.

The title compound, $\text{C}_{11}\text{H}_{11}\text{NO}_2$, was synthesized by chemo-selective *N*-acetylation of 4-aminophenol followed by reaction with propargyl bromide in the presence of K_2CO_3 . The acetamide and propyn-1-yloxy substituents form dihedral angles of $18.31(6)$ and $7.01(10)^\circ$, respectively, with the benzene ring. In the crystal, molecules are linked by $\text{N}-\text{H}\cdots\text{O}$ hydrogen bonds into chains along $[010]$. $\text{C}-\text{H}\cdots\text{O}$ and $\text{C}-\text{H}\cdots\pi$ interactions also occur.

Related literature

For background to the development of hybrid drug candidates against tuberculosis, malaria and cancer, see: Morphy *et al.* (2004). For details of the synthesis of the title compound, see: Hoogendoorn *et al.* (2011); Reppe (1955).



Experimental

Crystal data

$\text{C}_{11}\text{H}_{11}\text{NO}_2$
 $M_r = 189.21$

Monoclinic, $P2_1/c$
 $a = 13.973(2)$ Å

$b = 9.1794(13)$ Å
 $c = 7.5105(11)$ Å
 $\beta = 99.441(4)^\circ$
 $V = 950.3(2)$ Å³
 $Z = 4$

Mo $K\alpha$ radiation
 $\mu = 0.09$ mm⁻¹
 $T = 100$ K
 $0.3 \times 0.26 \times 0.23$ mm

Data collection

Bruker APEX DUO 4K CCD diffractometer
Absorption correction: multi-scan (SADABS; Bruker, 2008)
 $T_{\min} = 0.969$, $T_{\max} = 0.981$

6753 measured reflections
2388 independent reflections
2103 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.018$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.037$
 $wR(F^2) = 0.100$
 $S = 1.04$
2388 reflections
131 parameters

H atoms treated by a mixture of independent and constrained refinement
 $\Delta\rho_{\max} = 0.28$ e Å⁻³
 $\Delta\rho_{\min} = -0.24$ e Å⁻³

Table 1

Hydrogen-bond geometry (Å, °).

Cg1 is the centroid of the C4–C11 ring.

$D-\text{H}\cdots A$	$D-\text{H}$	$\text{H}\cdots A$	$D\cdots A$	$D-\text{H}\cdots A$
$\text{N1}-\text{H1}\cdots\text{O2}^{\text{i}}$	0.879 (14)	1.993 (14)	2.8695 (11)	175.2 (13)
$\text{C9}-\text{H9B}\cdots\text{O2}^{\text{i}}$	0.98	2.53	3.4043 (14)	148
$\text{C5}-\text{H5}\cdots\text{Cg1}^{\text{ii}}$	0.95	2.69	3.5171 (12)	146
$\text{C9}-\text{H9A}\cdots\text{Cg1}^{\text{iii}}$	0.98	2.94	3.7373 (12)	139

Symmetry codes: (i) $-x, y - \frac{1}{2}, -z - \frac{1}{2}$; (ii) $x, -y - \frac{1}{2}, z - \frac{1}{2}$; (iii) $-x, -y, -z$.

Data collection: APEX2 (Bruker, 2011); cell refinement: SAINT (Bruker, 2008); data reduction: SAINT and XPREP (Bruker, 2008); program(s) used to solve structure: SIR97 (Altomare *et al.*, 1999); program(s) used to refine structure: SHELXL97 (Sheldrick, 2008); molecular graphics: DIAMOND (Brandenburg & Putz, 2005); software used to prepare material for publication: WinGX (Farrugia, 1999).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: NC2291).

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supporting information

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N*-[4-(2-Propyn-1-yloxy)phenyl]acetamide*Yonas H. Belay, Henok H. Kinfe and Alfred Muller****S1. Comment**

In our pursuit in the development of hybrid drug candidates against tuberculosis, malaria and cancer (Morphy *et al.*, 2004), the title compound was identified as a building starting material. The compound was synthesized by chemoselective *N*-acetylation of 4-aminophenol followed by reaction with propargyl bromide in the presence of K_2CO_3 (Hoogendoorn *et al.*, 2011). To confirm the chemoselectivity, herein we report the single-crystal structure of the title compound.

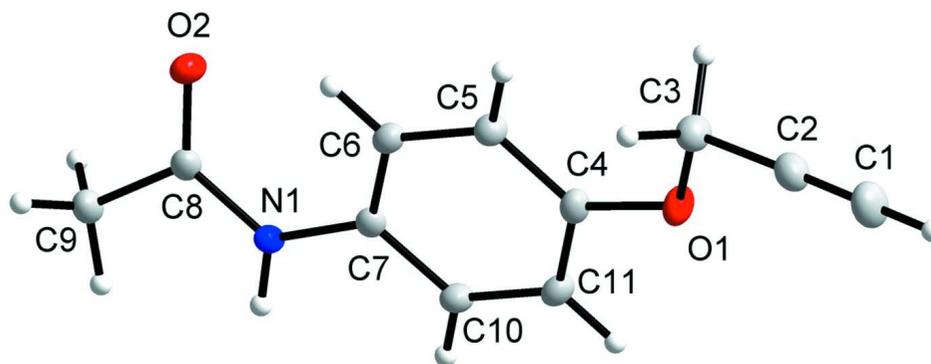
In the crystal structure of the title compound the acetamide and propyn-1-yloxy substituents form dihedral angles to the six-membered ring of $18.31 (6)^\circ$ and $7.01 (10)^\circ$ respectively (Figure 1). Molecules are linked by infinite one-dimensional $N-H\cdots O$ hydrogen bonding into chains that elongate in the [010] direction (see Figure 2 for a visual summary).

S2. Experimental

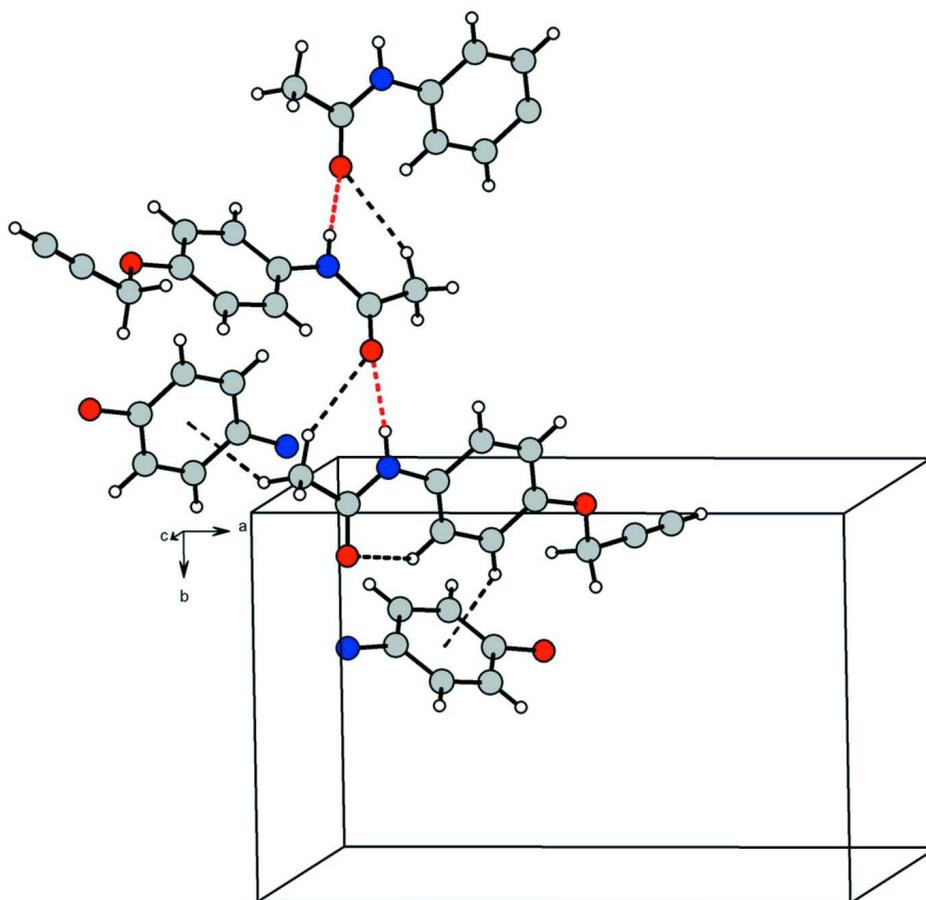
A solution of *N*-(hydroxy-phenyl)acetamide (450 mg, 2.980 mmol), synthesized by chemoselective acetylation of 4-aminophenol using 1 equivalence of acetic anhydride, in dry acetone was treated with potassium carbonate (576 mg, 4.17 mmol). The reaction mixture was stirred under reflux for about 30 minutes followed by addition of propargyl bromide (0.8 ml, 6.56 mmol). The combined solution was stirred for additional 3 h and concentrated under *vacuo*. The residue was diluted with water and extracted three times with ethyl acetate. The combined organic layer was washed with brine and water and dried over anhydrous sodium sulfate, filtered and solvent evaporated. The solid crude product was recrystallized from dichloromethane and hexane to afford 71% of the target compound as pale yellow crystals. The melting point of the crystalline material was found to similar as reported in literature (Reppe, 1955).

S3. Refinement

All hydrogen atoms were positioned in geometrically idealized positions with $C-H = 0.99 \text{ \AA}$ (methylene), 0.98 \AA (methyl) and 0.95 \AA (aromatic and acetylenic). The amide hydrogen atom were obtained from a Fourier difference map and refined with varying coordinates. All these hydrogen atoms were allowed to ride on their parent atoms with $U_{iso}(H) = 1.2U_{eq}$, except for methyl and amide hydrogen atoms where $U_{iso}(H) = 1.5U_{eq}$ was utilized. The initial positions of methyl hydrogen atoms were located from a Fourier difference map and refined as a fixed rotor.

**Figure 1**

Crystal structure of the title compound with labeling and displacement ellipsoids drawn at the 50% probability level..

**Figure 2**

Packing diagram showing the molecules linked by infinite one-dimensional N—H...O chains in the [010] direction. Hydrogen bonds and C—H...O/π interactions are shown as red and black dashed lines respectively.

N*-[4-(2-Propyn-1-yloxy)phenyl]acetamideCrystal data*C₁₁H₁₁NO₂ $M_r = 189.21$ Monoclinic, $P2_1/c$

Hall symbol: -P 2ybc

 $a = 13.973 (2) \text{ \AA}$ $b = 9.1794 (13) \text{ \AA}$ $c = 7.5105 (11) \text{ \AA}$ $\beta = 99.441 (4)^\circ$ $V = 950.3 (2) \text{ \AA}^3$ $Z = 4$ $F(000) = 400$ $D_x = 1.323 \text{ Mg m}^{-3}$ Mo $K\alpha$ radiation, $\lambda = 0.71073 \text{ \AA}$

Cell parameters from 3099 reflections

 $\theta = 2.7\text{--}28.4^\circ$ $\mu = 0.09 \text{ mm}^{-1}$ $T = 100 \text{ K}$

Block, pale yellow

 $0.3 \times 0.26 \times 0.23 \text{ mm}$ *Data collection*

Bruker APEX DUO 4K CCD

diffractometer

Graphite monochromator

Detector resolution: $8.4 \text{ pixels mm}^{-1}$ φ and ω scans

Absorption correction: multi-scan

(SADABS; Bruker, 2008)

 $T_{\min} = 0.969$, $T_{\max} = 0.981$

6753 measured reflections

2388 independent reflections

2103 reflections with $I > 2\sigma(I)$ $R_{\text{int}} = 0.018$ $\theta_{\text{max}} = 28.5^\circ$, $\theta_{\text{min}} = 2.7^\circ$ $h = -18 \rightarrow 18$ $k = -12 \rightarrow 11$ $l = -10 \rightarrow 10$ *Refinement*Refinement on F^2

Least-squares matrix: full

 $R[F^2 > 2\sigma(F^2)] = 0.037$ $wR(F^2) = 0.100$ $S = 1.04$

2388 reflections

131 parameters

0 restraints

Primary atom site location: structure-invariant

direct methods

Secondary atom site location: difference Fourier map

Hydrogen site location: inferred from neighbouring sites

H atoms treated by a mixture of independent and constrained refinement

 $w = 1/[\sigma^2(F_o^2) + (0.0509P)^2 + 0.3049P]$ where $P = (F_o^2 + 2F_c^2)/3$ $(\Delta/\sigma)_{\text{max}} < 0.001$ $\Delta\rho_{\text{max}} = 0.28 \text{ e \AA}^{-3}$ $\Delta\rho_{\text{min}} = -0.24 \text{ e \AA}^{-3}$ *Special details*

Experimental. The intensity data was collected on a Bruker Apex DUO 4 K CCD diffractometer using an exposure time of 20 s/frame. A total of 735 frames were collected with a frame width of 0.5° covering up to $\theta = 28.47^\circ$ with 99.3% completeness accomplished. Analytical data: mp: 110 - 111 °C (Lit. 109 - 111 °C; Reppe, 1955); ¹H NMR (CDCl₃, 400 MHz): d 7.57 (s, 1H), 7.38 (d, $J = 8.4 \text{ Hz}$, 2H), 6.89 (d, $J = 8.8 \text{ Hz}$, 2H), 4.63 (s, 2H), 2.49 (s, 1H), 2.12 (s, 3H); ¹³C NMR (CDCl₃, 400 MHz): d 168.4, 154.3, 131.9, 121.8, 115.3, 78.5, 75.5, 56.1, 24.4.

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

Refinement. Refinement of F^2 against ALL reflections. The weighted R -factor wR and goodness of fit S are based on F^2 , conventional R -factors R are based on F , with F set to zero for negative F^2 . The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R -factors(gt) etc. and is not relevant to the choice of reflections for refinement. R -factors based on F^2 are statistically about twice as large as those based on F , and R -factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	0.44065 (5)	0.09706 (8)	0.16260 (10)	0.01982 (18)
O2	-0.00853 (5)	0.27539 (8)	-0.14889 (10)	0.02019 (18)
N1	0.05791 (6)	0.05346 (9)	-0.18684 (12)	0.01555 (19)
C1	0.63468 (9)	0.09825 (14)	0.49415 (17)	0.0288 (3)
H1A	0.6943	0.0641	0.5601	0.035*
C2	0.56036 (8)	0.14084 (12)	0.41199 (15)	0.0215 (2)
C3	0.46720 (8)	0.19131 (12)	0.31532 (14)	0.0202 (2)
H3A	0.4174	0.1874	0.395	0.024*
H3B	0.4726	0.2931	0.2748	0.024*
C4	0.34482 (7)	0.09626 (11)	0.08432 (13)	0.0160 (2)
C5	0.27561 (7)	0.19574 (11)	0.12113 (13)	0.0165 (2)
H5	0.2934	0.2712	0.2068	0.02*
C6	0.17996 (7)	0.18471 (11)	0.03218 (13)	0.0160 (2)
H6	0.1327	0.2524	0.0582	0.019*
C7	0.15352 (7)	0.07514 (10)	-0.09429 (13)	0.0143 (2)
C8	-0.01572 (7)	0.15035 (11)	-0.20997 (13)	0.0156 (2)
C9	-0.10956 (7)	0.09587 (11)	-0.31599 (14)	0.0192 (2)
H9A	-0.1605	0.1005	-0.2407	0.029*
H9B	-0.1014	-0.0051	-0.353	0.029*
H9C	-0.1279	0.1568	-0.4233	0.029*
C10	0.22426 (7)	-0.02335 (11)	-0.13094 (14)	0.0169 (2)
H10	0.207	-0.0982	-0.2177	0.02*
C11	0.31883 (7)	-0.01321 (11)	-0.04271 (14)	0.0175 (2)
H11	0.3661	-0.0809	-0.0687	0.021*
H1	0.0464 (10)	-0.0325 (16)	-0.2373 (18)	0.021*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0138 (4)	0.0255 (4)	0.0184 (4)	0.0032 (3)	-0.0024 (3)	-0.0051 (3)
O2	0.0192 (4)	0.0149 (3)	0.0248 (4)	0.0026 (3)	-0.0015 (3)	-0.0008 (3)
N1	0.0139 (4)	0.0124 (4)	0.0192 (4)	-0.0008 (3)	-0.0006 (3)	-0.0010 (3)
C1	0.0196 (6)	0.0338 (6)	0.0302 (6)	-0.0025 (5)	-0.0039 (5)	0.0011 (5)
C2	0.0192 (5)	0.0236 (5)	0.0211 (5)	-0.0036 (4)	0.0014 (4)	-0.0027 (4)
C3	0.0190 (5)	0.0213 (5)	0.0189 (5)	0.0002 (4)	-0.0010 (4)	-0.0032 (4)
C4	0.0136 (5)	0.0190 (5)	0.0148 (4)	0.0012 (4)	0.0000 (4)	0.0021 (3)
C5	0.0168 (5)	0.0165 (4)	0.0154 (4)	0.0005 (4)	0.0003 (4)	-0.0022 (3)
C6	0.0162 (5)	0.0150 (4)	0.0168 (5)	0.0020 (4)	0.0022 (4)	0.0000 (3)
C7	0.0140 (5)	0.0138 (4)	0.0146 (4)	-0.0001 (3)	0.0007 (3)	0.0027 (3)
C8	0.0146 (5)	0.0156 (4)	0.0162 (4)	-0.0001 (3)	0.0014 (4)	0.0032 (3)
C9	0.0147 (5)	0.0184 (5)	0.0234 (5)	-0.0007 (4)	-0.0006 (4)	0.0018 (4)
C10	0.0181 (5)	0.0139 (4)	0.0179 (5)	0.0004 (4)	0.0006 (4)	-0.0017 (3)
C11	0.0171 (5)	0.0159 (4)	0.0191 (5)	0.0040 (4)	0.0016 (4)	-0.0002 (4)

Geometric parameters (Å, °)

O1—C4	1.3713 (12)	C5—C6	1.3965 (14)
O1—C3	1.4360 (12)	C5—H5	0.95
O2—C8	1.2340 (12)	C6—C7	1.3911 (13)
N1—C8	1.3495 (13)	C6—H6	0.95
N1—C7	1.4152 (13)	C7—C10	1.3999 (14)
N1—H1	0.879 (14)	C8—C9	1.5036 (14)
C1—C2	1.1840 (17)	C9—H9A	0.98
C1—H1A	0.95	C9—H9B	0.98
C2—C3	1.4582 (15)	C9—H9C	0.98
C3—H3A	0.99	C10—C11	1.3807 (14)
C3—H3B	0.99	C10—H10	0.95
C4—C5	1.3903 (14)	C11—H11	0.95
C4—C11	1.3922 (14)		
C4—O1—C3	116.86 (8)	C5—C6—H6	119.8
C8—N1—C7	127.50 (9)	C6—C7—C10	118.96 (9)
C8—N1—H1	117.0 (9)	C6—C7—N1	124.10 (9)
C7—N1—H1	115.5 (9)	C10—C7—N1	116.92 (9)
C2—C1—H1A	180	O2—C8—N1	123.46 (9)
C1—C2—C3	178.14 (12)	O2—C8—C9	121.13 (9)
O1—C3—C2	107.39 (8)	N1—C8—C9	115.41 (9)
O1—C3—H3A	110.2	C8—C9—H9A	109.5
C2—C3—H3A	110.2	C8—C9—H9B	109.5
O1—C3—H3B	110.2	H9A—C9—H9B	109.5
C2—C3—H3B	110.2	C8—C9—H9C	109.5
H3A—C3—H3B	108.5	H9A—C9—H9C	109.5
O1—C4—C5	124.98 (9)	H9B—C9—H9C	109.5
O1—C4—C11	115.11 (9)	C11—C10—C7	120.87 (9)
C5—C4—C11	119.90 (9)	C11—C10—H10	119.6
C4—C5—C6	119.98 (9)	C7—C10—H10	119.6
C4—C5—H5	120	C10—C11—C4	119.94 (9)
C6—C5—H5	120	C10—C11—H11	120
C7—C6—C5	120.34 (9)	C4—C11—H11	120
C7—C6—H6	119.8		
C4—O1—C3—C2	161.20 (9)	C8—N1—C7—C10	-162.01 (10)
C3—O1—C4—C5	11.37 (14)	C7—N1—C8—O2	-0.68 (16)
C3—O1—C4—C11	-169.65 (9)	C7—N1—C8—C9	179.68 (9)
O1—C4—C5—C6	179.65 (9)	C6—C7—C10—C11	0.40 (15)
C11—C4—C5—C6	0.72 (15)	N1—C7—C10—C11	-177.99 (9)
C4—C5—C6—C7	-0.44 (15)	C7—C10—C11—C4	-0.13 (15)
C5—C6—C7—C10	-0.12 (14)	O1—C4—C11—C10	-179.47 (9)
C5—C6—C7—N1	178.15 (9)	C5—C4—C11—C10	-0.44 (15)
C8—N1—C7—C6	19.69 (15)		

Hydrogen-bond geometry (Å, °)

Cg1 is the centroid of the C4–C11 ring.

<i>D</i> —H··· <i>A</i>	<i>D</i> —H	H··· <i>A</i>	<i>D</i> ··· <i>A</i>	<i>D</i> —H··· <i>A</i>
N1—H1···O2 ⁱ	0.879 (14)	1.993 (14)	2.8695 (11)	175.2 (13)
C6—H6···O2	0.95	2.31	2.8816 (13)	118
C9—H9B···O2 ⁱ	0.98	2.53	3.4043 (14)	148
C5—H5···Cg1 ⁱⁱ	0.95	2.69	3.5171 (12)	146
C9—H9A···Cg1 ⁱⁱⁱ	0.98	2.94	3.7373 (12)	139

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