

Scientific paper

An Axial Chirality and Disorder of Positional Isomers in a Crystal of Highly Cytotoxic 3-acetyl-1,3-bis(2-chloro-4-nitrophenyl)-1*E*-triazene

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Dedicated to the memory of Prof. Dr. Jurij V. Brenčič.

Abstract

Biologically active 4-nitro-substituted 1,3-diaryltriazene, a chemical analogue of 1,3-bis(4'-amidinophenyl)-triazene-berenil[®], belongs to the novel, chemically modified class of potent antitumor agents. Its structural characterization by X-ray analysis and ¹H NMR spectroscopy is performed to determine molecular overall conformation in view of its possible interaction to DNA.

Keywords: Axial chirality, Enantiomeric disorder, Molecular structure, Crystal structure

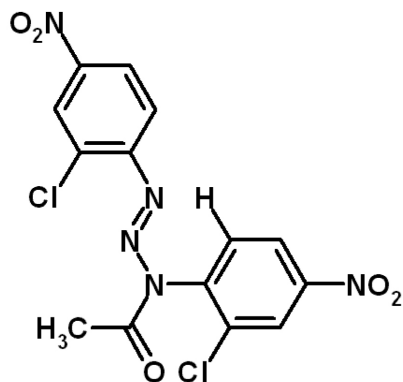
1. Introduction

The synthesis and biological activity of a new class of 4-nitro-substituted 1,3-diaryltriazenes have revealed that this class can be modified from inactive to highly cytotoxic compounds by substitution of the two nitro groups at the *para* position of benzene rings and two additional electron withdrawing groups at the *ortho* position.^{1,2} To increase solubility of these compounds the triazene nitrogen was acetylated, however, LC-MS/MS analysis pointed out that *N*-acyltriazenes are prodrugs of non-acylated triazenes. This class of compounds exhibit anticancer activity. The selected representative of this group, 3-acetyl-1,3-bis(2-chloro-4-nitrophenyl)-1*E*-triazene preferentially targets malignant cells. Since its antiproliferative activity is significantly higher against tumor cells than against normal cells, the above mentioned compound may serve as a potential antitumor agent.¹ DNA binding analysis suggests that 3-acetyl-1,3-bis(2-chloro-4-nitrophenyl)-1*E*-triazene and its non-acylated derivative do not bind into the minor groove of DNA.¹ Instead, it induces reactive oxygen species and the endoplasmic stress response, as well as independent activation of stress-activated protein kinase/*c*-Jun NH₂-terminal kinase (SAPK/JNK) pathway.^{1,3}

Various triazenes have been synthesized and thoroughly investigated over a few decades due to their potential in human and veterinary medicine.⁴ and references therein However, their mechanisms of activity at molecular level have not been clarified yet. Among all triazenes, binding mode of berenil, 1,3-bis(4'-amidinophenyl)-triazene, has been examined experimentally and by molecular modelling that proved heterogeneous DNA-binding modes.⁵ However, the generally accepted mode of berenil binding is *via* complexation into the minor-groove of the A-T reach domains of DNA double helices and also RNA.^{6,7} Some other stereochemically feasible berenil-DNA complexes can be modelled with the drug partially intercalated through the minor groove or pseudo-intercalated through the major groove.⁵ Both models revealed the global helical parameters of DNA similar to the same DNA in the absence of the drug and in the original crystal structure of the decamer.^{5,8} In addition to this classic duplex minor groove binding, G-quadruplex binding was reported, recently;⁹ the experiments also revealed that berenil is not as selective for AT-rich duplexes as previously thought. Its inhibiting activity of topoisomerases was established as well.^{10,11}

Therefore, among of all 4-nitro-substituted 1,3-diaryltriazenes synthesized, we selected 3-acetyl-1,3-

bis(2-chloro-4-nitrophenyl)-1*E*-triazene (Scheme 1), as the most cytotoxic against different tumor cell lines,¹ to determine its molecular structure and overall conformation in the solid state by X-ray structure analysis and ¹H NMR spectroscopy. Its molecular structure should provide structural evidences why the title compound is not suitable for an intercalation into DNA.



Scheme 1

2. Results and Discussion

The molecular graph (Scheme 1) indicates that the title molecule cannot be planar due to a steric hindrance and its crystal structure reveals strongly non-planar mo-

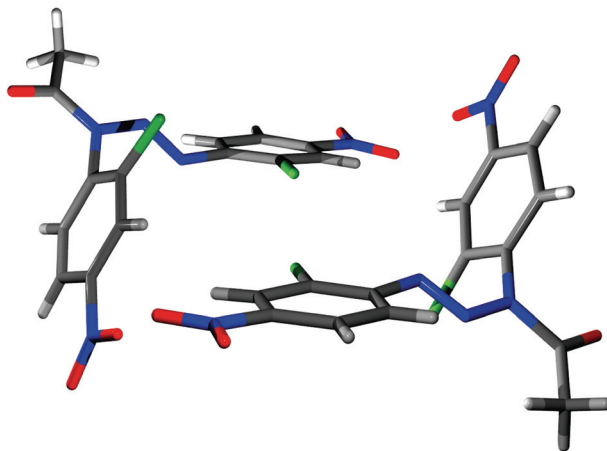


Figure 1. An asymmetric unit with the two molecules A and B related by a pseudo-inversion centre.

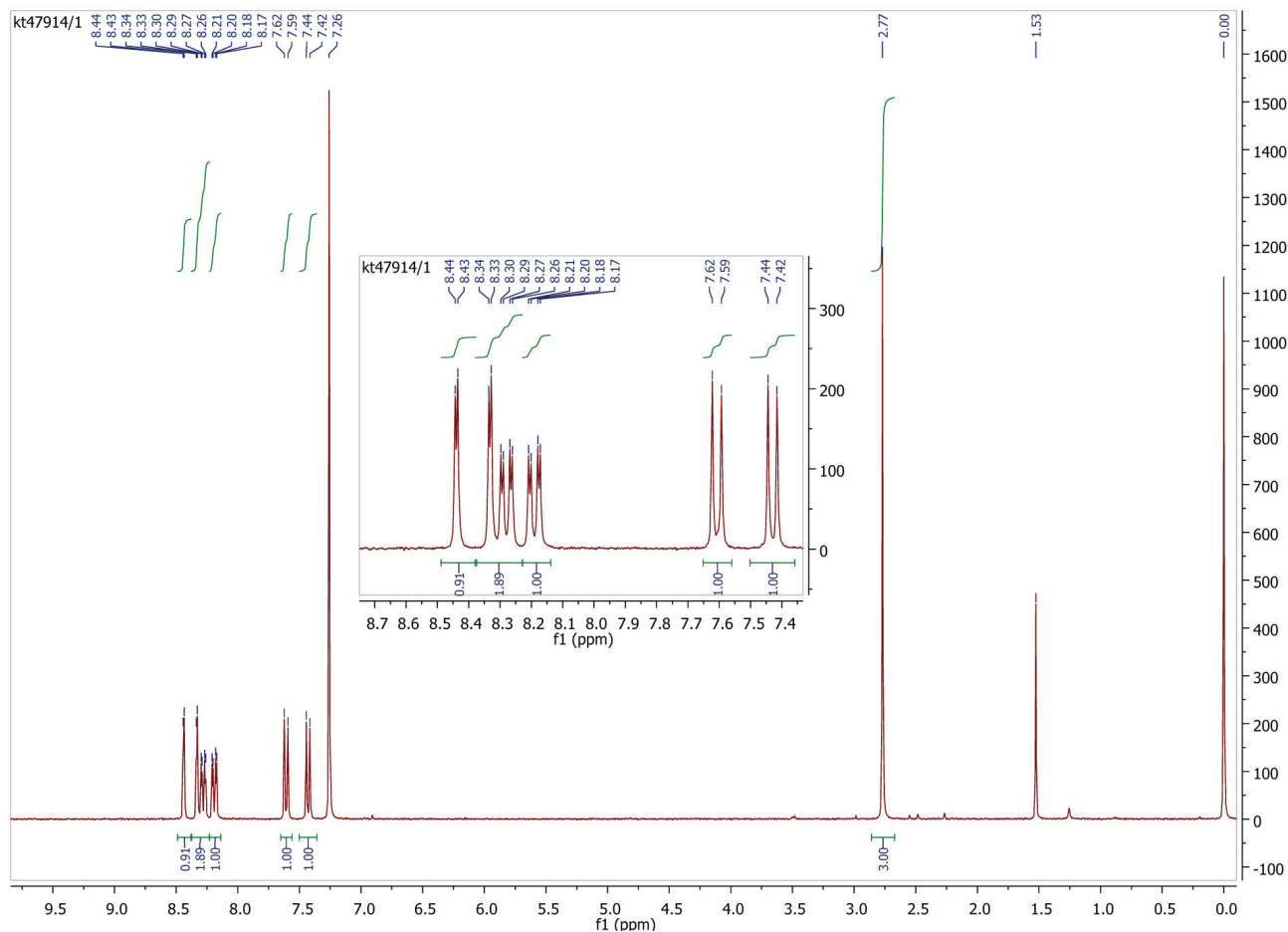
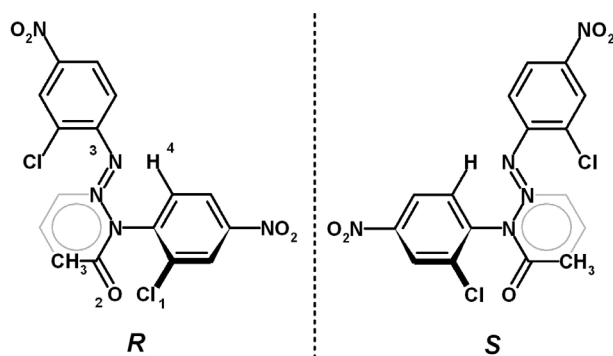


Figure 2. ¹H NMR spectrum of 3-acetyl-1,3-*bis*(2-chloro-4-nitrophenyl)-1*E*-triazene in CDCl₃ solution.

Table 1. Torsional angles defining enantiomeric relations of *R-A* and *S-B* molecules.

	<i>S-A</i>	<i>R-A</i>	<i>R-B</i>	<i>S-B</i>
·C11/H3–C3–C4–N2	–5.70 (12)	5.70 (12)	4.27 (12)	–4.27 (12)
·C12/H5–C5–C4–N2	–11.9 (16)	11.9 (16)	–3.2 (12)	3.2 (12)
C3–C4–N2–N3	–75.6 (14)	75.6 (14)	–78.4 (12)	78.4 (12)
C5–C4–N2–N3	103.1 (13)	–103.1 (13)	100.5 (11)	–100.5 (11)
C4–N2–N3–N4	6.1 (13)	–6.1 (13)	3.8 (12)	–3.8 (12)
N2–N3–N4–C7	–177.7 (7)	177.7 (7)	–178.7 (7)	178.7 (7)
N3–N4–C7–C8	147.6 (8)	–147.6 (8)	141.8 (8)	–141.8 (8)

·Two different orientations of the ring (resulting in atropisomers), require the atom sequences to start with different atoms.



Scheme 2. Chirality of the title compound can be described in analogy to substituted biphenyls. The planar moiety N=N-N-CO-CH₃ can be regarded as a fragment of a substituted phenyl ring (indicated in gray). Due to a hindered rotation, midpoints of N2–C4(phenyl) bonds can be regarded as a stereogenic centre; four different substituents are -H, -Cl, =N and =O and their priority is indicated defining the absolute configuration of axially chiral molecule. The numbers assigned to atoms assign the priority important for defining the absolute configuration according to CIP rules.^{13–15}

lecular conformation. The dihedral angles between two planes of the aryl groups in both conformers characterize puckered molecules [67.2(5)° in molecule **A** and 62.3(5)° in molecule **B**]. Two symmetry-independent molecules (**A** and **B** in the asymmetric unit) (Fig. 1) are related by a pseudo-inversion centre located approximately at (0.75, 0.12, 0.12). Conformations of **A** and **B** are nearly identical within experimental error (the differences in torsional angles are about 3 uncertainty units, Table 1). Due to the presence of the pseudo-inversion centre, **A** and **B** molecules are almost in an enantiomeric relationship.

A hindered intramolecular rotation around N-C_{phenyl} bond leads to a disorder of the phenyl ring vicinal to the acetyl group in order to optimize the crystal packing. The chlorine atom is disordered over two positions, so that a half of a chlorine atom is bound to each α -C atom of the ring. Therefore, the two isomers are present, occupying the same crystallographic position (both occupancies are 50%). However, they could not be distinguished by NMR spectra, as no splitting of the signals was detected (Fig. 2, Section 4.1). The only explanation can be that the molecu-

le is chiral: the two disordered isomers observed in the crystal structure are actually enantiomers and the crystals are racemic.

Chiral molecules lacking asymmetrically substituted atom(s) are usually referred to as axially chiral or helical.^{12–14} In many compounds similar to biphenyls intramolecular rotation which would transform a left- into a right-handed conformer is hindered due to sterically bulky substituents. Such conformers which may be stable at room temperature are referred to as atropisomers. In some cases, such as chiral biphenyls and allenes, a stereogenic centre (not necessarily an atom) may be defined and an absolute configuration may be designated according to CIP-rules.^{13–15} The »stereogenic centre« is located at the midpoint of the central C–C bond, and *R/S* configuration is determined by positions of the four substituents, analogous to the configurations of the tetrahedral carbon atom. Due to non-planarity of the title compound and hindered intramolecular rotation, such a centre can be recognised at the midpoint of C4–N2 bond (Scheme 1, Fig. 3). Due to sterical reasons, rotation around the bond is hindered. The phenyl ring and the N=N-N-CO-CH₃ moiety are planar and conformationally rigid; therefore the N=N-N-CO-CH₃ moiety can also be regarded as a fragment of the phenyl ring (Scheme 2). Four different substituents are identified around the C4–N2 bond: H and Cl are bound to the phenyl, while =N and =O are bound to the NNC »phenyl fragment« (Scheme 2). Priorities are assigned to these substituents according to the CIP-rules. Therefore, *R* and *S* configurations can be assigned to different conformations of the molecules **A** and **B** according to the CIP-rules (Scheme 2).

Generally, any object (molecule) in a 3D space is chiral if it comprises four non-equivalent non-coplanar points (atoms). The four points may be linked by three non-coplanar vectors, which span either a left- or a right-handed coordinate system; alternatively, three non-coplanar vectors define a fragment of a left- or a right-handed helix. Since both *R*- and *S*-enantiomers of each molecule (**A** and **B**) are present, the four molecules can be described in the asymmetric unit (Fig. 3) and can be designated either as (*R-A*, *S-B*) or (*R-B*, *S-A*).

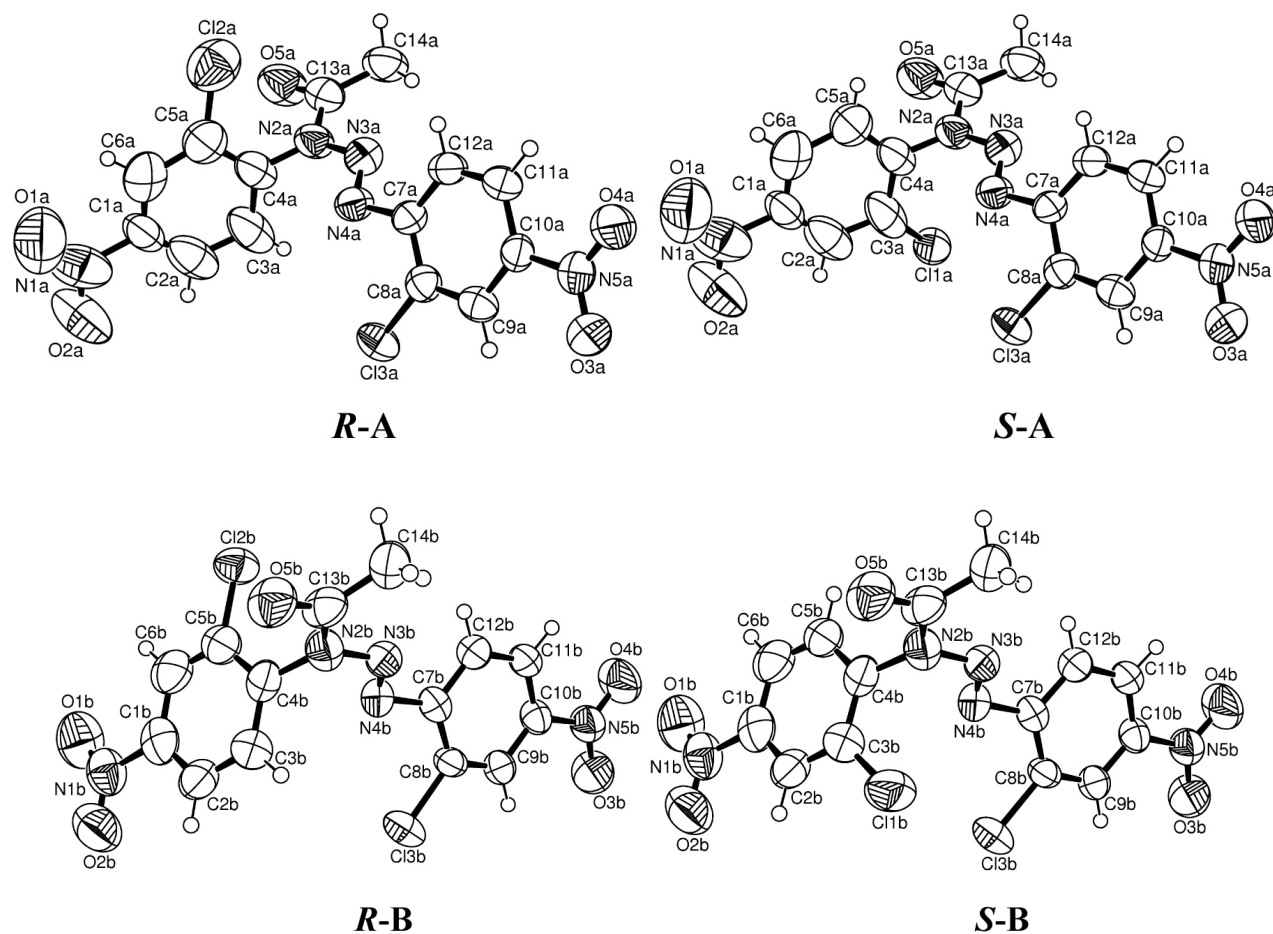


Figure 3. ORTEP-3¹⁶ drawings of two atropisomers (left and right) of two symmetry-independent molecules (**A** and **B**). Displacement ellipsoids are drawn for the probability of 50% and hydrogen atoms are shown as spheres of arbitrary radii.

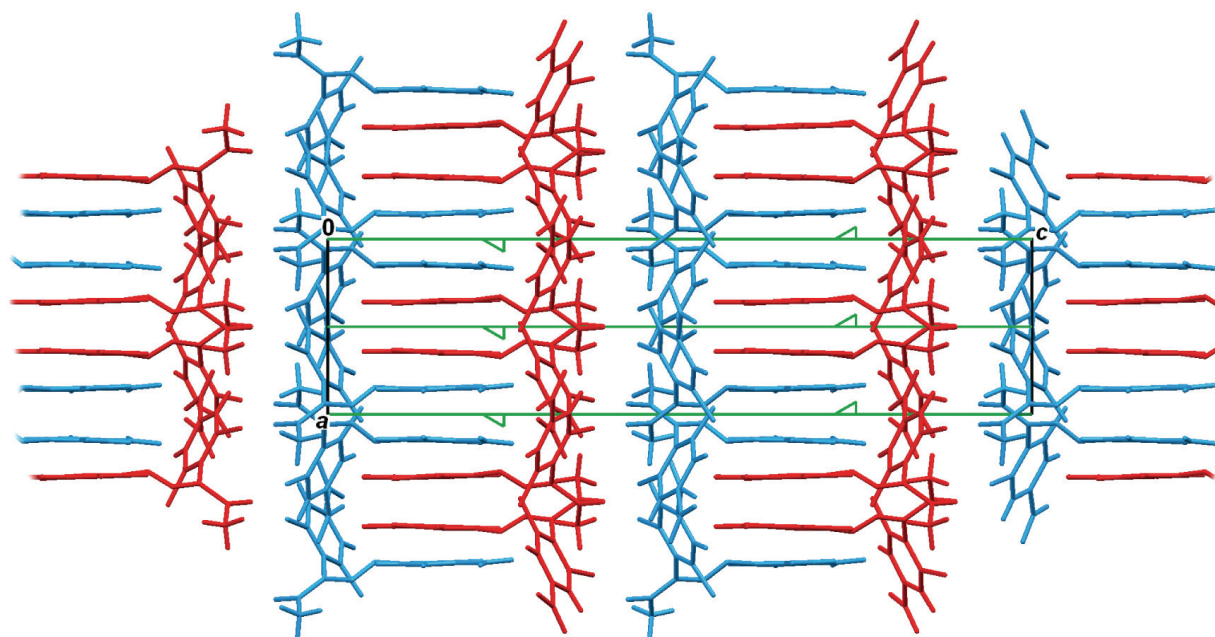


Figure 4. Crystal packing of **1** viewed down the direction [010]. For clarity, only enantiomeric pair of **A** (red) and **B** (blue) molecules are shown; hydrogen bonds have been omitted. Screw-twofold axes are shown in green.

Table 2. Geometric parameters of hydrogen bonds.

	$D-H / \text{\AA}$	$H \cdots A / \text{\AA}$	$D \cdots A / \text{\AA}$	$D-H \cdots A / ^\circ$	Symm. op. on A
C9A–H9A \cdots O2B	0.93	2.56	3.427(15)	156	x, y, z
C14A–H14A \cdots Cl2A	0.96	2.50	3.449(13)	170	$-1+x, y, z$
C14B–H14E \cdots Cl2B	0.96	2.56	3.483(13)	162	$1+x, y, z$
C14B–H14F \cdots Cl2A	0.96	2.82	3.724(13)	157	$2-x, -y, -1/2+z$

Table 3. Geometric parameters of the $\pi \cdots \pi$ interactions

$\pi \cdots \pi$	$Cg^a \cdots Cg / \text{\AA}$	α^b	β^c	$Cg \cdots \text{plane}(Cg2) / \text{\AA}$	Offset / \AA	Symm. Op.
C7A \rightarrow C12A \cdots C7B \rightarrow C12B	3.810 (5)	1.6 (4)	20.81	3.537 (4)	1.353	$1-x, 1/2+y, z$
C7B \rightarrow C12B \cdots C7A \rightarrow C12A	3.792 (5)	1.6 (4)	20.54	3.576 (4)	1.328	$2-x, 1/2+y, z$

a Cg = centre of gravity of the aromatic ring.

b α = angle between planes of two aromatic rings.

c β = angle between Cg \cdots Cg line and normal to the plane of the first aromatic ring.

The title molecule reveals no strong proton donors, thus 3D packing is achieved through C–H \cdots O and C–H \cdots Cl hydrogen bonds and dispersion interactions (Fig. 4). Phenyl rings C7 \rightarrow C12 (non-disordered ones) form π -stacks extending in the direction [100] (Tables 2 and 3).

3. Conclusion

A sterical hindrance (overcrowding effect) brings the molecule into non-planar conformation, that leads to the axial chirality. A less-common case of disorder, including the two positional isomers, occurs. The two disordered molecules were detected in the asymmetric unit (**A** and **B**) being related as two enantiomeric pairs of molecules. The significantly puckered molecule of the title compound prevents its intercalation into DNA duplex as also revealed by biological evaluation, suggesting other events to cause cell death.¹

4. Experimental

Melting point was determined on a Kofler micro hot stage and is uncorrected. ¹H NMR spectrum was recorded with a Bruker Avance DPX 300 spectrometer at 29 °C and 300 MHz, using TMS as an internal standard. ¹³C NMR spectrum was recorded on the same instrument at 75.5 MHz and is referenced against the central line of the solvent signal (DMSO-*d*₆ septet at $\delta = 39.5$ ppm). IR spectrum was obtained with Bio-Rad FTS 3000MX (KBr pellet). MS spectrum was recorded with a VG-Analytical AutoSpec Q instrument. Elemental analysis (C, H, N) was performed with Perkin Elmer 2400 Series II CHNS/O Analyzer.

4. 1. Synthesis and Characterization Data

(i) *Synthesis of the starting material*: A solution of sodium nitrite (2 mmol, 0.141 g) in water (5 mL) was added to the stirring suspension of the commercially available 2-chloro-4-nitroaniline (4 mmol, 0.704 g) in hydrochloric acid (5%, 8.6 mL) over the period of 10 min at 0 °C. The reaction mixture was stirred at r.t. for 24 hours. Then, it was cooled to 0 °C, the product was filtered off and washed with water (1 mL). The crude 1,3-bis(2-chloro-4-nitrophenyl)-1*E*-triazene (0.576, 81% yield) was crystallized from acetone. Mp 199–200 °C; IR (KBr) 3098, 1585, 1528, 1509, 1341, 1242, 1171, 1118, 1047, 869 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.83 (2H, d, $J = 9.0$ Hz), 8.22 (dd, 2H, $J_1 = 9.0$ Hz, $J_2 = 2.4$ Hz), 8.39 (2H, d, $J = 2.4$ Hz), 10.47 (1H, s).

(ii) *Synthesis of 3-acetyl-1,3-bis(2-chloro-4-nitrophenyl)-1*E*-triazene*: Acetyl chloride (282.6 mg, 3.6 mmol) was added dropwise to the suspension of 1,3-bis(2-chloro-4-nitrophenyl)-1*E*-triazene (712 mg, 2 mmol) and triethylamine (405 mg, 4 mmol) in acetonitrile (10 mL) at room temperature. The reaction mixture was stirred at the same temperature for 15 min and the solid (triethylammonium chloride) was filtered off. Then, the solution was evaporated to 3–4 mL and methanol (10 mL) was added. The crude product was separated by filtration (684 mg, 86% yield) and crystallized from methanol/acetone. Mp 145–147 °C; IR (KBr) 3100, 1733, 1523, 1470, 1350, 1193, 1139 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 2.77 (3H, s), 7.43 (1H, d, $J = 8.6$ Hz), 7.60 (1H, d, $J = 8.6$ Hz), 8.19 (1H, dd, $J_1 = 8.6$ Hz, $J_2 = 2.5$ Hz), 8.28 (1H, dd, $J_1 = 8.6$ Hz, $J_2 = 2.5$ Hz), 8.33 (1H, d, $J = 2.5$ Hz), 8.43 (1H, d, $J = 2.5$ Hz); ¹³C NMR (75 MHz, DMSO-*d*): δ 22.2, 120.7, 123.3, 123.6, 124.7, 125.6, 130.8, 132.4, 133.1, 139.5, 147.5, 148.6, 148.9, 171.9; MS (EI) m/z 397 (M⁺, 0.1), 184 (100), 156 (83),

110 (33), 75 (30). Anal. for $C_{14}H_9Cl_2N_5O_5$: Calcd C, 42.32; H, 2.27; N, 17.63. Found C, 42.35; H, 2.37; N, 17.34.

4. 2. Crystallography

Single crystal measurements were performed on an Enraf-Nonius CAD-4 diffractometer, using a graphite monochromated $CuK\alpha$ (1.54179 Å) radiation at room temperature [293(2) K]. Three intensity control reflections measured every 120 minutes. The WinGX standard procedure was applied for data reduction.¹⁷ No absorption correction was applied. The structure was solved using SHELXS97¹⁷ and refined with SHELXL97.¹⁸ The model was refined using the full-matrix least squares refinement; all non-hydrogen atoms were refined anisotropically. Hydrogen atoms were treated as constrained entities, using the command AFIX in SHELXL97.¹⁸ Molecular geometry calculations were performed by PLATON,¹⁹ and molecular graphics were prepared using ORTEP-3,¹⁶ and CCDC-

Mercury.²⁰ Crystallographic and refinement data for the structure reported in this paper are show in Table 4.

Supplementary crystallographic data for this paper can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk). CCDC-773227 contains the supplementary crystallographic data for this paper.

5. Acknowledgements

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6. References

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Table 4. Crystallographic, data collection and structure refinement details.

Compound	1
Empirical formula	$C_{14}H_9Cl_2N_5O_5$
Formula wt. / g mol ⁻¹	398.16
Crystal dimensions / mm	0.40 × 0.09 × 0.07
Space group	$Pbc2_1$
<i>a</i> / Å	7.1152 (5)
<i>b</i> / Å	16.3138 (7)
<i>c</i> / Å	28.683 (2)
α / °	90
β / °	90
γ / °	90
<i>Z</i>	8
<i>V</i> / Å ³	3329.4 (4)
<i>D</i> _{calc} / g cm ⁻³	1.589
μ / mm ⁻¹	3.876
Θ range / °	3.08–76.32
<i>T</i> / K	293 (2)
Diffractometer type	Enraf-Nonius CAD-4
Range of <i>h</i> , <i>k</i> , <i>l</i>	0 < <i>h</i> < 8;
0 < <i>k</i> < 20;	
–36 < <i>l</i> < 0	
Reflections collected	3555
Independent reflections	3555
Observed reflections (<i>I</i> ≥ 2 σ)	2010
Absorption correction	None
<i>R</i> _{int}	0
<i>R</i> (<i>F</i>)	0.0634
<i>R</i> _w (<i>F</i> ²)	0.2009
Goodness of fit	1.033
H atom treatment	Constrained
No. of parameters	489
$\Delta\rho_{\max}$, $\Delta\rho_{\min}$ (eÅ ⁻³)	0.357; –0.205
Flack parameter	0.06 (4)

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Povzetek

Biološko aktiven 4-nitro-substituiran 1,3-diariltriazen, analog berenila[®] [1,3-bis(4'-amidinofenil)-triazena], spada v novo, kemijsko modificirano skupino učinkovitih antitumornih spojin. Njegove strukturne značilnosti smo študirali z rentgensko strukturno analizo in z ¹H NMR spektroskopijo, da bi ugotovili celotno konformacijo in možnost morebitne interakcije z DNA.

checkCIF/PLATON report

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 8b

Bond precision: C-C = 0.0150 A Wavelength=1.54184
Cell: a=7.1152(5) b=16.3138(7) c=28.6832(19)
 alpha=90 beta=90 gamma=90
Temperature: 293 K

	Calculated	Reported
Volume	3329.4(4)	3329.4(4)
Space group	Pbc21	P b c 21
Hall group	P 2c -2b	P 2c -2b
Moiety formula	C14 H8 Cl2 N5 O5	C14 H9 Cl2 N5 O5
Sum formula	C14 H8 Cl2 N5 O5	C14 H9 Cl2 N5 O5
Mr	397.15	398.16
Dx,g cm-3	1.585	1.589
Z	8	8
Mu (mm-1)	3.875	3.876
F000	1608.0	1616.0
F000'	1618.80	
h,k,lmax	8,20,36	8,20,36
Nref	3562[6976]	3555
Tmin,Tmax	0.691,0.762	
Tmin'	0.202	


Correction method= Not given


Data completeness= 1.00/0.51 Theta(max)= 76.320

R(reflections)= 0.0634(2010) wR2(reflections)= 0.2009(3555)

S = 1.033 Npar= 489

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

 **Alert level B**
PLAT340_ALERT_3_B Low Bond Precision on C-C Bonds (x 1000) Ang .. 15

 **Alert level C**
PLAT089_ALERT_3_C Poor Data / Parameter Ratio (Zmax .LT. 18) 7.27
PLAT230_ALERT_2_C Hirshfeld Test Diff for N1A -- C1A .. 6.64 su

PLAT230_ALERT_2_C Hirshfeld Test Diff for C1A -- C2A .. 5.17 su
 PLAT241_ALERT_2_C Check High Ueq as Compared to Neighbors for C3A
 PLAT242_ALERT_2_C Check Low Ueq as Compared to Neighbors for N5A
 PLAT242_ALERT_2_C Check Low Ueq as Compared to Neighbors for C1A
 PLAT242_ALERT_2_C Check Low Ueq as Compared to Neighbors for N1B
 PLAT366_ALERT_2_C Short? C(sp?)-C(sp?) Bond C4A - C5A ... 1.36 Ang.
 PLAT366_ALERT_2_C Short? C(sp?)-C(sp?) Bond C2B - C3B ... 1.37 Ang.
 PLAT041_ALERT_1_C Calc. and Reported SumFormula Strings Differ ?
 PLAT042_ALERT_1_C Calc. and Reported MoietyFormula Strings Differ ?
 PLAT068_ALERT_1_C Reported F000 Differs from Calcd (or Missing)... ?
 PLAT234_ALERT_4_C Large Hirshfeld Difference N2A -- C13A .. 0.16 Ang.
 PLAT234_ALERT_4_C Large Hirshfeld Difference C1A -- C6A .. 0.22 Ang.
 PLAT234_ALERT_4_C Large Hirshfeld Difference C3A -- C4A .. 0.22 Ang.
 PLAT234_ALERT_4_C Large Hirshfeld Difference C1B -- C2B .. 0.18 Ang.
 PLAT234_ALERT_4_C Large Hirshfeld Difference C4B -- C5B .. 0.18 Ang.
 PLAT234_ALERT_4_C Large Hirshfeld Difference C5B -- C6B .. 0.15 Ang.

Alert level G

FORMU01_ALERT_2_G There is a discrepancy between the atom counts in the
 _chemical_formula_sum and the formula from the _atom_site* data.
 Atom count from _chemical_formula_sum: C14 H9 Cl2 N5 O5
 Atom count from the _atom_site data: C14 H8 Cl2 N5 O5
 CELLZ01_ALERT_1_G Difference between formula and atom_site contents detected.
 CELLZ01_ALERT_1_G WARNING: H atoms missing from atom site list. Is this intentional?
 From the CIF: _cell_formula_units_Z 8
 From the CIF: _chemical_formula_sum C14 H9 Cl2 N5 O5
 TEST: Compare cell contents of formula and atom_site data

atom	Z*formula	cif sites	diff
C	112.00	112.00	0.00
H	72.00	64.00	8.00
Cl	16.00	16.00	0.00
N	40.00	40.00	0.00
O	40.00	40.00	0.00

REFLT03_ALERT_4_G WARNING: Large fraction of Friedel related reflns may
 be needed to determine absolute structure
 From the CIF: _diffrn_reflns_theta_max 76.32
 From the CIF: _reflns_number_total 3555
 Count of symmetry unique reflns 3562
 Completeness (_total/calc) 99.80%
 TEST3: Check Friedels for noncentro structure
 Estimate of Friedel pairs measured 0
 Fraction of Friedel pairs measured 0.000
 Are heavy atom types Z>Si present yes
 PLAT072_ALERT_2_G SHELXL First Parameter in WGHT Unusually Large.. 0.10
 PLAT301_ALERT_3_G Note: Main Residue Disorder 4.00 Perc.
 PLAT860_ALERT_3_G Note: Number of Least-Squares Restraints 4
 PLAT128_ALERT_4_G Non-standard setting of Space-group Pca21 Pbc21
 PLAT199_ALERT_1_G Check the Reported _cell_measurement_temperature 293 K
 PLAT200_ALERT_1_G Check the Reported _diffrn_ambient_temperature 293 K
 PLAT380_ALERT_4_G Check Incorrectly? Oriented X(sp2)-Methyl Moiety C14A
 PLAT380_ALERT_4_G Check Incorrectly? Oriented X(sp2)-Methyl Moiety C14B

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- 0 ALERT level A = In general: serious problem
 - 1 ALERT level B = Potentially serious problem
 - 18 ALERT level C = Check and explain
 - 12 ALERT level G = General alerts; check

7 ALERT type 1 CIF construction/syntax error, inconsistent or missing data

10 ALERT type 2 Indicator that the structure model may be wrong or deficient
4 ALERT type 3 Indicator that the structure quality may be low
10 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 13/08/2009; check.def file version of 12/08/2009

Datablock 8b - ellipsoid plot

