Crystal Structure and Hirshfeld Surface Analysis of 1,4-Pentadien-3-one, (1E,4E)-1,5-diphenyl-2-(2,4-dinitrophenyl)hydrazone

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The compound 1,4-pentadien-3-one, (1E,4E)-1,5-diphenyl-2-(2,4-dinitrophenyl)hydrazone presents the molecular formula C_{23}H_{18}N_{4}O_{4} and was prepared in an undergraduate laboratory. The hydrazone was synthesized from the condensation between dibenzalacetone and 2,4-dinitrophenylhydrazine (DNPH) and crystallized employing water/acetone liquid-liquid diffusion. The structure presents three aromatic rings connected by an unsaturated Y-shaped system. Dinitro substituted and one of the other aromatic rings are 15° out of a coplanarity, while the other phenyl group is almost orthogonal to the first (89°). The only observed classical hydrogen bonding is an intramolecular N–H···O. The supramolecular structure was analyzed employing the Hirshfeld surface and that is organized through C-H···O hydrogen bond and C-H···π, polar-π, and π-stacking. An interaction involving NO2···NO2 was also observed.

Keywords: crystal structure, 2,4-dinitrophenylhydrazine, hydrazone

Introduction

Hydrazones are privileged structures in medicinal chemistry. They possess pharmacological activities like analgesic, anticonvulsant, antidepressant, anti-inflammatory and antiplatelet, antimalarial, antimicrobial, antiviral, and vasodilator.1,2 Hydrazone formation is a traditional identification and purification method (Brady’s test)3 for aldehydes and ketones, thus we have prepared the compound 1,4-pentadien-3-one, (1E,4E)-1,5-diphenyl-2-(2,4-dinitrophenyl)hydrazone (1) as part of an undergraduate laboratory course by an established method employing accessible reagents.4 More recently, new applications of the hydrazone formation are the measurement of formaldehyde indoor or in cigarettes,5,6 removal of acrolein from active pharmaceutical ingredients (APIs)7 and finally the removal of aldehydes and ketones from essential oils by using a scavenger resin.8 The hydrazone (1) is easily synthesized, and crystallization provides large single crystals employing different methods and solvent systems. Such aspects raise this hydrazone as an excellent example of crystallography teaching that can be extended to different aldehydes and ketones.

Experimental

Synthesis

Acetone, absolute ethanol, sulfuric acid PA (Vetec, Rio de Janeiro, Brazil) and 2,4-dinitrophenylhydrazine (Merck KGaA, Darmstadt, Germany) were used without further purification. Dibenzalacetone was prepared as described in the literature.4 The compound 1 (Scheme 1) was prepared from condensation between 2,4-dinitrophenylhydrazine (DNPH) and dibenzalacetone (1,5-diphenyl-1,4-pentadien-3-one): in an Erlenmeyer of 125 mL under magnetic stirring, 1.0 g of dibenzalacetone (4.3 mmol) was dissolved in 40 mL of H_2SO_4 and added to a mixture of 60 mL of water and 200 mL of ethanol. Then, 30 mL of the 2,4-DNPH acid solution was added into the dibenzalacetone mixture while stirring at room temperature for 15 min. After the time, the reaction mixture was filtered over a Buchner filter to obtain a red powder, then washed with cold
ethanol. The amorphous solid was transferred to another Erlenmeyer and recrystallized from a mixture of water and acetone to produce crystals of pure dibenzalacetone-2,4-dinitrophenylhydrazone. Single crystals as red prisms were obtained by slow diffusion of water through an acetone solution containing the compound 1.

2,4-Dinitrophenylhydrazine is sensitive to shock and friction and can be explosive when dry and it is a flammable solid. It is supplied damp or ‘wetted’, and it is important to keep it wet, so the current storage advice is to keep it in a sealed container, which is itself kept in an outer container filled with a small amount of water.9

X-ray diffraction (XRD) single crystal analysis was conducted in a Bruker Venture II diffractometer employing Cu Kα radiation. Absorption was corrected by multi-scan method (SADABAS).10 Data was collected until 0.83 Å of resolution, and it was indexed in the monoclinic crystalline system and in the P21/c space group, with Z (formula unit per unit cell) = 4 and Z’ (formula unit per asymmetric unit) = 1. Structure determination was done through directed methods with the software SHELXS inserted in the WinGX platform.11,12 Refinement was realized with full-matrix least-square method implemented in SHELXL.13 Model convergence was attained with R-factor (residual factor for 3214 reflections or discrepancy index) of 0.046, R_w (weighted R-factor) of 0.131, and S (goodness of fit) of 1.06. All non-hydrogen atoms were localized through the electron density map and anisotropically refined. N–H hydrogen was located from a difference-Fourier map and refined without constrains. Other H atoms were included in the final cycles of refinement using a riding model, with Uiso(H) = 1.2Ueq(C). Geometry data and figures were obtained with the software PLATON14 and Mercury.15 Hirshfeld and electron density surfaces, and fingerprint plot were obtained with Crystal Explorer.16,17 Crystallographic data for the structure in this work were deposited in the Cambridge Crystallographic Data Centre (CCDC) with number 2009611. Crystal data and refinement information are shown in Table 1 and in Supplementary Information section. The molecular structure of compound 1 can be seen in Figure 1a with thermal ellipsoids.

Results and Discussion

Dibenzalacetone was chosen as starting material as it is easily obtained after the aldol reaction between benzaldehyde and acetone, and it was already performed in the undergraduate laboratory. The compound 1 was easily and safely prepared in an undergraduate laboratory using quite non-expensive materials. Moreover, the easy

Figure 1. Molecular structure of the compound 1: (a) displacement ellipsoids at 50% of probability and (b) aromatic rings configuration.
crystallization provided large single crystals employing different methods and solvent systems. The combination of synthesis and crystallization render this activity as an example of crystallography teaching, allows for improvement of the undergraduate curricula, and can be further extended to different aldehydes and ketones according to inventory availability.

The structure presents three aromatic rings, designated as A, B, and C (Figure 1b). A and B are almost orthogonal and their idealized least-square (LS) planes form an angle of 88.930(47)°. A and C are more coplanar and their ideal LS planes form an angle of 14.926(64)°. Dinitro substituted aromatic ring A is flat and exhibits the smallest HOMA (harmonic oscillator model of aromaticity) index (rms 0.0056, deviation from the idealized least-square planes; HOMA_A: 0.873). The orthogonal B is the most aromatic one (rms 0.0049; HOMA_B: 0.988), while the C ring presents slightly smaller local aromaticity when compared with B (rms 0.0053; HOMA_C: 0.976). Coplanar part of the unsaturated Y-like system (between A and C) exhibits slightly more equalized bonds than the orthogonal side, denoting better electronic conjugation between A and C.

Intramolecular hydrogen bonding leads to the formation of a six-membered planar ring (rms 0.0338) between hydrazone N-H and the ortho nitro group oxygen (Table 2). Hydrogen position (close to the nitrogen) was obtained from difference Fourier map (F_o - F_calc) and refined isotopically. Hydrogen bonding geometry is consistent with that described to other dinitrophenyl hydrazones like salicylaldehyde 2,4-dinitrophenylhydrazone (CCDC reference code BAFGUL01), 20 4-(1-(2-(2,4-dinitrophenyl)hydrazino)butylidene)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one N,N-dimethylformamide solvate (ZAKCAS), 21  and (1E)-1-(3-bromophenyl)ethanone 2,4-dinitrophenylhydrazone (VABCUY). 22  The structure of 2,4-DNPH (W ASRAJ01) was redetermined in 2006. 23  A partially quinoidal structure for DNPH was suggested due to the low equalization of C-C aromatic bonds (HOMA calculated from data: 0.831), specially ortho-quinoidal. Here we observed some similar partial quinoidal behavior within A ring but is a less extend.

| Table 1. Crystallographic information |
|--------------------------------------|
| Crystal color/habit | red, prism |
| Crystal size / mm | 0.45 x 0.07 x 0.04 |
| Empirical formula | C_{23}H_{18}N_{4}O_{4} |
| Formula weight / (g mol^{-1}) | 414.41 |
| F(000) | 864.0 |
| Temperature / K | 100 |
| Absorption coefficient / mm^{-1} | 0.81 |
| Calculated density / (g cm^{-3}) | 1.393 |
| Wavelength / Å | 15.1306(10) |
| a, b, c / Å | 12.8166(9) |
| α, β, γ / degree | 90.000 |
| Crystal system | monoclinic |
| Space group | P2_1/c |
| Volume / Å^3 | 1976.0(2) |
| Z, Z' | 4, 1 |
| Diffractometer | Bruker D8 Venture APEX-III |
| Data collection | φ and ω scans on KAPPA goniometer |
| Reflections collected | 26308 |
| Independent reflections | 3473 |
| Absorption correction | multi-scan |
| T_{min}, T_{max} | 0.611, 0.753 |
| Theta range for data collection / degree | 4.53 to 68.372 |
| Index ranges | -18 < h < 18 |
| -15 < k < 14 |
| -12 < l < 12 |
| Data/restraints/parameters | 34730/284 |
| Goodness-of-fit on F^2 | 1.06 |
| Final residual factor [I > 2σ(I)] | R_I: 0.0464 |
| | wR_I: 0.1270 |
| Residual factor (all data) | R_F: 0.0490 |
| | wR_F: 0.1306 |
| H-atom treatment | a mixture of independent and constrained refinement |
| Largest diff. peak and hole / (e Å^{-3}) | 0.27, −0.25 |

| Table 2. Hydrogen bond geometry |
|----------------------------------|
| D--H--A | Symmetry operation | D--H | H--A | D--A | D--H--A |
| N1--H1A--O1 | – | 0.89(2) | 1.89(2) | 2.6146(17) | 127.4(18) |
| C5--H5--O2 | 1 + x, 1/2 + y, 3/2 − z | 0.9500 | 2.5700 | 3.494(2) | 166.00 |
| C6--H6--O3 | 1 + x, 1/2 + y, 3/2 − z | 0.9500 | 2.5200 | 3.4655(19) | 170.00 |
| C23--H23--O4 | 1 + x, 1/2 + y, 3/2 − z | 0.9500 | 2.5500 | 3.451(2) | 158.00 |

D.A: hydrogen bond donator and acceptor.
Hydrogen atoms of the dinitro-substituted A and nitro groups oxygens exhibit intermolecular self-assembly through C–H···O bonds giving rise to parallel linear polymeric tapes that grow along b axis (Figure 2). Distances in H···O contacts varies in the range 2.52-2.57 Å, shorter than the sum of van der Waals radii (2.72 Å), and indicate high directionality. They are organized by pairs of DD-AA interactions (D,A: hydrogen bond donator and acceptor) that give origin to rings with 11 (blue), 12 (orange), and 14 (yellow) members (Figure 2a). The overall graph set can be described as C4 H4[6][R22(11), R32(12), R22(14)].

C–H···O hydrogen bonds connect linearly each molecule to the other three. Fingerprint plot in Figure 3 demonstrates that H···O/O···H contacts are responsible for 24.2% of the Hirshfeld surface, with the formation of two sharp features and a broad blue area in the Hirshfeld surface. The polymeric tapes pile up with layering formation is prevented due to out of plane B-ring configuration, that establish CH···π and π···π interactions (Figure 2b). Intermolecular hydrogen bonds geometry data can be found in Table 2.

Nitro function presents a higher electronic density over both oxygens, which enable this group to act as Lewis base accepting hydrogen bonds. In Figure 4a the electrostatic potential was plotted over an electron density surface and the red-colored oxygens emerged surrounded by hydrogen atoms. This group, however, exhibit also a positive electrostatic portion described as a π-hole over the C–N bond. This π-hole presents Lewis acid character and establishes an intermolecular interaction with oxygen from the nitro group, with N···O distance of 3.027 Å, slight smaller than the sum of the van der Waals radii (3.07 Å). In the Figure 4a the complementary electrostatic character of the NO2···NO2 interaction is displayed. Each molecule of compound 1 is connected to the other two by the means of nitro contacts, giving origin to a zig-zag chain motif observed along b axis in Figure 4b.

A polar-π almost parallel offset interaction was observed between A and B rings, with centroids separation of 3.9601(9) Å and the horizontal displacement of 2.127 Å; (the angle formed between the planes was 4.25°). Two of these supramolecular interactions are intermediated by one A···A parallel offset with centroids distance of 4.4809(9) Å, with horizontal displacement of the planes of 3.106 Å. Orthogonal B rings show a parallel offset π···π interaction toluene-like with centroids distance of 3.7985(10) Å (horizontal displacement of 1.598 Å). In the fingerprint plot, C···C interactions give origin to the light blue portion in the 1.8 vs. 1.8 π-stacking region (Figure 3). B ring π···π contact is sandwiched between two C–H···π hydrogen bonds. These π interactions are summarized in Figure 5.

Despite exhibiting one basic nitrogen (from hydrazone group), the participation of N···H/H···N interactions are almost negligible in the supramolecular structure, probably because of steric effects.

The crystal packing view along b axis is displayed in Figure 6. It is possible to observe alternation between the A-ring hydrogen-bonded motif and B-ring with π interactions.

A search in the Cambridge Structural Database (CSD, version 5.41, 2020.0 CSD, last update November 2019) through the software CONQUEST with the keyword “hydrazone” returned 1661 hits. Delimiting the search to dinitrophenyl hydrazone, a total of 191 hits were found. Most of the structures exhibit both nitro groups and the aromatic ring in a flat (or near flat) configuration. In the vast majority of these crystal structures, an intramolecular hydrogen bond was observed between hydrazone N–H and oxygen from nitro at the ortho position. Notable exceptions were the derivatives of 6-chloro-2,4-dinitrophenylhydrazine.

Figure 2. Polymeric linear motif formed by self-assembly of the aromatic cores; (a) thermal ellipsoids at 50% of probability, view down a axis; (b) space-filling model displaying C–H···O pattern.
Such hydrazones present both chlorine and nitro substituents in the ortho positions, but the ortho group adopts a different orientation, far from N–H and with about 60° of torsion. Some examples are EDUJAO, EDUJES, EDUJOC, and GANQAO. MOGUL analysis revealed that most of the structural aspects of compound 1 find similarities with
related hydrazones. Some aspects concerned with C7 neighborhood, although are unusual: the angle formed by C7–N2–N1 fragment, of 116.17° (the average is 118.45° among 15 related hits). The torsion angle of 116.51° in the fragment C9–C8–C7–N2 is also unusual (common angle is closer to 180°). Such unusual aspects can be attributed to the presence of two phenylethene moieties bonded to C7.

**Conclusions**

A combination of synthesis and crystallization was employed to obtain single crystals of a hydrazone. The red prisms obtained represents a crystallography demonstration to improve undergraduate curricula.

**Supplementary Information**

Crystallographic data (excluding structure factors) for the structures in this work were deposited in the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 2009611. Copies of the data can be obtained, free of charge, via [https://www.ccdc.cam.ac.uk/structures/](https://www.ccdc.cam.ac.uk/structures/).

Supplementary crystallographic data are available free of charge at [http://jbcs.sbq.org.br](http://jbcs.sbq.org.br) as PDF file.
Acknowledgments

We would like to acknowledge professor Pierre M. Esteves, Lygia de Moares and Ministério da Ciência, Tecnologia, Inovações e Comunicações (MCTIC), Financiadora de Estudos e Projetos (FINEP), LDRX (Laboratório Multiusuário de Difração de Raios-X da UFF), and Centro Nacional de Biologia Estrutural e Bioimagem (CENABIO) for the support with the X-ray diffraction facility (D8-Venture).

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Submitted: June 13, 2020
Published online: September 30, 2020

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