Synthesis and crystal structures of 7,8-bromo (dibromo) -3-tert-butylpyrazolo[5,1-c][1,2,4]triazines

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Abstract

Single crystal structures in a series of 7-bromo-, 8-bromo-, and 7,8-dibromo-3-tert-butylpyrazolo[5,1-c][1,2,4]triazin-4(1H)-ones have been investigated by X-ray diffraction. Novel 7-bromo- and 7,8-dibromo-3-tert-butylpyrazolo[5,1-c][1,2,4]triazines were synthesized by reduction of triazine carbonyl with dehydrative aromatization in acidic media, and their XRD structural features were compared with that of the 4-oxo analogs. The lengths and bond angles and the packing of molecules in crystals have been considered. Non-valence interactions for some of the studied compounds were observed. Correlations between the presence of bromine atoms at different positions and structural features are determined.

Keywords Crystal structure, X-ray diffraction, 1,2,4-Triazine, Pyrazolo[5,1-c] [1,2,4]triazine

Introduction

The qualitative and quantitative structural aspects of heterocyclic compounds are of interest in terms of their utility for the certain mechanistic and synthetic studies [1–3], as well as for various biological applications [4–6]. It is known that most of the six-membered saturated heterocycles prefer the chair conformations [7, 8], while the aromatics are nearly planar. The significant deviations can often be the result of combination of steric and electronic factors [9].

Fused triazines exhibit diverse conformational behavior depending on the nature of an annulated ring [10, 11]. Azolo[1,2,4] triazines [12] constitute an important class of such compounds which have found broad use as effective antiviral agents, e.g., 1,2,4-triazolo[5,1-c][1,2,4]triazine (triazavirin) [13] and pyrrolo[2,1-f][1,2,4]triazine (remdesivir) [14, 15]. Nevertheless, the structural features of such systems are still relatively poorly studied. In continuation of our studies on the chemical and structural properties of functionalized pyrazolo[5,1-c][1,2,4]triazines [16–21], in the present work, we discuss the single crystal structures in a series of brominated 4-oxo- and novel 4-unsubstituted-3-tert-butylpyrazolo[5,1-c][1,2,4]triazines, including bond lengths and angles, non-valence interactions, and packing modes.

Experimental

General experimental remarks

Melting points were determined on a STUART Melting point SMP30 apparatus. IR spectra were recorded in KBr pellets using Agilent Cary 660 FTIR infrared spectrophotometer. NMR spectra were recorded on Bruker AM-300 or AV-600 spectrometers operating at working frequencies of 300 (1H), 75 or 151 MHz (13C). Chemical shifts were related to that of the CHCl3 (1H), or CDCl3 (13C). High resolution mass spectra were recorded on a Bruker MicroTOF II instrument in positive ion mode (capillary voltage 4500 V) using electrospray ionization (ESI) and methanol or acetonitrile as a solvent. Elemental analysis was performed on a PerkinElmer Series II 2400 Elemental Analyzer. All reagents were obtained from commercial sources and used without additional purification. Starting compounds 1a,b, 2a-d, and 3a were synthesized as described in literature (Scheme 1) [17–20].
Reagents and conditions:

i: KOH or K₂CO₃, EtOH/H₂O, NBu₄⁺Br⁻ (cat.), 20–100 °C, then HCl/H₂O, 0 °C (for 1b only);

ii: MeOH or i-PrOH or neat (for 3a only), t-BuONO, Δ 5–15 min;

iii: NBS, Et₃N, EtOAc or MeCN, 0–25 °C, 5 min – 1 h;

iv: TMSBr/t-BuONO, MeCN, Δ 15 min;

v: NaH, THF, 20°C, 15 min, then n-BuLi, THF, –97 °C, 3 min, then KH₂PO₄, H₂O, 0 °C;

vi: B₂H₆, Et₂O/THF, 10–20 °C, 7 h;

vii: BH₃/ BF₃, Et₂O/THF, 0–20 °C, 2 weeks.

Scheme 1

**General procedure for the synthesis of compounds 3b and 3c (Scheme 2)**

Compound 1b (1.23 g, 4.90 mmol) was dissolved in a mixture of DMF (10 ml), NEt₃ (1 ml, 7.17 mmol), and Boc₂O (1.1 g, 5.04 mmol). To the resulting solution, NaN₃ (10 mg, 1.53 × 10⁻⁴ mol) was added, and the reaction mixture was heated at 60 °C for 15 min with stirring. Then, it was cooled and added to 100 ml of water. The formed precipitate was filtered, washed with H₂O (3 × 50 ml) and heptane (2 × 15 ml), dried

Reagents and conditions:

i: Boc₂O, NaN₃, NBu₄⁺Br⁻ (cat.), dioxane or DMF, 40–80 °C, 20–40 min, then TMSBr, t-BuONO, MeCN, 0–50 °C, 1.5 h (68%); ii: NaBH₄, MeOH, r.t. – 50 °C, 1 h, then HCl/H₂O, 0 °C – r.t., 2 h, then Na₂HPO₄, H₂O, r.t., 20 min (15–42% from 1b).

Scheme 2
### Table 1: Crystal data, data collection, and structure refinement for compounds 2a-d

| Compound | 2a | 2b | 2c | 2d-DMSO | 2d |
|----------|----|----|----|--------|----|
| Formula  | C₉H₁₁BrN₄O | C₉H₁₀Br₂N₄O | C₉H₁₁BrN₄O | C₉H₁₀BrN₂O,S | C₉H₁₁BrN₄O |
| M(®)     | 271.13 | 350.03 | 271.13 | 363.28 | 285.15 |
| Crystal system | Monoclinic | orthorhombic | Triclinic | Triclinic | Orthorhombic |
| Space group | P2₁/c | Pnca | P₁ | P₁ | Pnca |
| Unit cell dimensions | | | | | |
| a (Å) | 13.0854(3) | 11.1612(3) | 9.9149(5) | 6.9289(2) | 11.6416(2) |
| b (Å) | 7.4580(2) | 12.1198(3) | 11.5754(6) | 10.2508(3) | 12.0120(2) |
| c (Å) | 11.7128(3) | 12.1650(6) | 17.1209(4) | 11.7436(3) | 17.1040(3) |
| V (Å³) | 1118.52(5) | 2417.38(10) | 1101.58(10) | 793.54(4) | 2401.09(7) |
| Z | 4 | 8 | 4 | 2 | 8 |
| Δρ (max, e Å⁻³) | 3.653 | 6.710 | 3.711 | 3.410 | 1.578 |
| Δρ (min, e Å⁻³) | 0.653 | 2.112 | 0.999 | 2.112 | 1.578 |
| τm (°C) | 90.135(3) | 102.5990(10) | 90.135(3) | 102.5990(10) | 90.135(3) |
| Volume, Å³ | 2345.15(13) | 1140.78(12) | 1029.01(4) | 7446 | 3567 |
| μ (mm⁻¹) | 3.655 | 6.710 | 3.711 | 3.410 | 1.578 |
| T(°K) | 964 | 90 | 90 | 90 | 90 |
| g | 408 | 560 | 560 | 560 | 560 |
| hkl range (°) | 2.310 to 33.176 | 2.917 to 30.998 | 3.055 to 33.170 | 3.055 to 33.170 | 3.055 to 33.170 |
| Crystal data, data collection, and structure refinement for compounds 2a-d

### Table 2: Crystal data, data collection, and structure refinement for compounds 3a-c

| Compound | 3a | 3b | 3c |
|----------|----|----|----|
| Formula  | C₁₀H₁₃BrN₄ | C₉H₁₀Br₂N₄ | C₉H₁₁BrN₄ |
| M(®)     | 269.15 | 334.03 | 255.13 |
| Crystal system | orthorhombic | monoclinic | monoclinic |
| Space group | Pnma | P₂₁/m | P₂₁/m |
| Unit cell dimensions | | | |
| a (Å) | 17.6328(6) | 6.8857(4) | 6.05670(10) |
| b (Å) | 6.7165(2) | 7.3453(4) | 12.7391(3) |
| c (Å) | 19.8019(7) | 22.5552(14) | 13.6146(3) |
| V (Å³) | 2345.15(13) | 1140.78(12) | 1029.01(4) |
| Z | 8 | 4 | 4 |
| Δρ (max, e Å⁻³) | 3.655 | 6.710 | 3.711 |
| Δρ (min, e Å⁻³) | 0.653 | 2.112 | 0.999 |
| τm (°C) | 90.135(3) | 102.5990(10) | 90.135(3) |
| Volume, Å³ | 2345.15(13) | 1140.78(12) | 1029.01(4) |
| μ (mm⁻¹) | 3.655 | 6.710 | 3.711 |
| T(°K) | 964 | 90 | 90 |
| g | 408 | 560 | 560 |
| hkl range (°) | 2.310 to 33.176 | 2.917 to 30.998 | 3.055 to 33.170 |
| Crystal data, data collection, and structure refinement for compounds 3a-c
in air, and suspended in a mixture of TMSBr (4 ml, 30.31 mmol) and MeCN (10 ml). To this suspension, t-BuONO (5 ml, 42.04 mmol) was added dropwise over 20 min and with vigorous stirring. After the addition was complete, the black reaction mixture was further stirred for 1 h at 50 °C. After cooling to r.t., MeOH (15 ml) and NaBH₄ (1 g, 26.43 mmol) were simultaneously added in small portions with stirring over 30 min. After the addition was complete, the mixture was further stirred at 50 °C for 30 min. Then, it was cooled to 0 °C, conc. HCl/H₂O solution (15 ml) was added slowly, and the red reaction mixture was stirred for 2 h at r.t. Next, H₂O (100 ml), Na₂HPO₄·2H₂O (20 g, 112.37 mmol), EtOAc (30 ml), and heptane (50 ml) were added in one portion, and the biphasic mixture was stirred vigorously for 20 min at r.t. The organic phase was separated, dried with crystalline K₂CO₃ and anhydrous MgSO₄, and filtered. The solvents were removed in vacuo, and the residue was purified by two-fold flash column chromatography (eluted with EtOAc:heptane = 1:100 – 3:200) to give compounds 3b and 3c.

7,8-Dibromo-3-tert-butylpyrazolo[5,1-c][1,2,4]triazine (3b)

Yellow crystals, yield 0.68 g (2.04 mmol, 42%), mp. 124–125 °C. IR (KBr) ν = 3098, 3068, 2959, 2973, 2904, 2867 (CH), 1614, 1579, 1512, 1468, 1413, 1364, 1336, 1311, 1282, 1249, 1227, 1199, 1165, 1075, 1025, 934, 950, 874, 765, 729, 645 cm⁻¹. ¹H NMR: (300 MHz, CDCl₃) δ 8.31 (s, 1H, C(4)H), 1.55 (s, 9H, C(CH₃)₃). ¹³C{¹H} NMR: (151 MHz, CDCl₃) δ 154.61, 145.92, 136.54 (C(3), C(7), C(8a)), 116.45 (C(4)H), 89.25 (C(8)), 35.04 (C(CH₃)₃), 29.10 (C(CH₃)₃). HRMS m/z (Irel. %) calculated: 334.9325 [M+H]+, found: 334.9332 [M+H]+ (100). Anal. calcd. for C₉H₁₀Br₂N₄ (%): C, 32.36, H, 3.02, N, 16.77. Found (%): C, 32.40, H, 3.05, N, 16.72.

7-Bromo-3-tert-butylpyrazolo[5,1-c][1,2,4]triazine (3c)

Yellow crystals, yield 0.19 g (0.74 mmol, 15%), mp. 112–113 °C. IR (KBr) ν = 3137, 3067, 3015, 2974, 2961, 2930, 2900, 2867 (CH), 1832, 1566, 1579, 1546, 1510, 1462, 1416, 1369, 1312, 1334, 1283, 1230, 1249, 1196, 1144, 1117, 1073, 1027, 966, 928, 853, 821, 796, 753, 723, 663, 628, 554, 510, 439 cm⁻¹. ¹H NMR: (300 MHz, CDCl₃) δ 8.34 (s, 1H, C(4)H), 7.23 (s, 1H, C(8)H), 1.55 (s, 9H, C(CH₃)₃). ¹³C{¹H} NMR: (75 MHz, CDCl₃, 298 K) δ 154.33, 149.66, 135.41 (C(3), C(7), C(8a)), 116.72 (C(4)H), 100.80 (C(8)H), 35.48 (C(CH₃)₃), 29.73 (C(CH₃)₃). HRMS m/z (Irel. %) calculated: 255.0240 [M+H]+, found: 255.0245 [M+H]+ (100). Anal. calcd. for C₉H₁₁BrN₄ (%): C, 42.37, H, 4.35, N, 21.96. Found (%): C, 42.33, H, 4.38, N, 21.94.

For X-ray single crystal studies, all compounds were re-crystallized by slow solvent evaporation at r.t. from nearly saturated solutions in ethyl acetate/dimethylsulfoxide mixture (10:1 v/v). Crystallization of 2d from the same solvent mixture provided a mixture of two polymorph modifications: 2d·DMSO (major component, colorless blocks on a flask’s bottom, over 95%) and non-solvated 2d (minor, colorless blocks on flask’s walls).

Fig. 1 Molecular structures of 2a, 2c and 3c. H-atoms of methyl groups for 2a and 3c are omitted; displacement ellipsoids are shown at the 50% probability level

Fig. 2 Molecular structures of 2d, 2d-DMSO, and 3a, and packing of compound 3a in a single crystal. H-atoms of methyl groups for 2d and 3a are omitted; displacement ellipsoids are shown at the 50% probability level
**X-ray data collection and refinement**

X-ray diffraction data were collected at 100 K on a Bruker Quest D8 diffractometer equipped with a Photon-III area-detector (graphite monochromator, shutterless $\varphi$- and $\omega$-scan technique), using Mo K$_\alpha$ radiation (0.71073 Å). The intensity data were integrated by the SAINT program [22] and corrected for absorption and decay using SADABS [23]. The structure was solved by direct methods using SHELXT [24] and refined on $F^2$ using SHELXL-2018 [25].

For $2a,b,d$, $2d$-DMSO, and $3a$: all non-hydrogen atoms were refined with individual anisotropic displacement parameters. The locations of atom H1 in $2a,b,d$, $2d$-DMSO, and all hydrogen atoms in $3a$ were found from the electron density-difference map; they were refined with individual isotropic displacement parameters. All other hydrogen atoms were placed in ideal calculated positions and refined as riding atoms with relative isotropic displacement parameters. The molecule of non-solvated $2d$ is disordered over 2 positions with the ratio of 0.9613(6):0.0387(6).

For $2c$ and $3b,c$: all non-hydrogen atoms were refined with anisotropic displacement parameters. Positions of atoms H1A and H1B in $2c$ were found from the electron density-difference map and were restrained at the distance of 0.84(3) Å from N1A/N1B, correspondingly. All other hydrogen atoms in $2c$ and $3b,c$ were placed in ideal calculated positions and refined as riding atoms with relative isotropic displacement parameters. A rotating group model was applied for methyl groups in $2c$. The studied crystal of $2c$ was refined as a 2-component twin with the domain ratios of 0.407(2):0.593(2) and the twin law of (1.00 0.55 0.98, 0.00 -1.00 0.00, 0.01 0.00 -1.00) (the second major domain is rotated from the first one by 179.9° about reciprocal axis 1 0 0).

The SHELXTL program suite [22] was used for molecular graphics. Displacement ellipsoids are set to the 50% probability level on all figures below. See Electronic Supplementary Material (ESM) for more details on X-ray data collection and refinement.

Crystal data, data collection, and structure refinement details for $2a-d$ and $3a-c$ are summarized in Tables 1 and 2. Bond distances and angles, as well as additional ORTEP drawings, are presented in ESM for this paper. The structures have been deposited at the Cambridge Crystallographic Data Center with the reference CCDC numbers 2065233-2065240; they also contain the supplementary crystallographic data. These data can be obtained free of charge from the CCDC via [http://www.ccdc.cam.ac.uk/data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

**Results and discussion**

**Synthesis**

The starting compounds $1a,b$ were prepared by cyclocondensation of 4-amino-6-tert-butyl-3-methylsulfanyl-1,2,4-triazin-5-one with cyanoacetic acid derivatives in pyridine (Scheme 1) [18]. Hydrolysis of the pyrazole ester moiety in $1a$ and diazotization using tert-butyl nitrite gave 7-unsubstituted acid, which is converted to compound $2a$ by halodecarboxylation [17]. Alternatively, treatment of $1a,b$ with trimethylsilylbromide/t-BuONO followed by bromination or selective reduction of the CO$_2$Et group with diborane led to compounds $2b$ or $2d$, respectively [18, 19]. Compound $2c$ [18] was prepared by a selective C(8)-site Li/Br exchange in $2b$ using n-butyl lithium at low temperature, and further protonation.

Aromatic triazine $3a$ was synthesized from $2d$ by reduction/oxidative nitration sequence [19]. In order to further investigate the structural effects of bromine substitution on the aromatic pyrazolo[5,1-c][1,2,4]triazine system, we set the task of switching the oxygen atom to hydrogen at the C4 position and comparing the structure of the obtained compounds. Novel 4-unsubstituted pyrazolotriazines $3b,c$ were prepared by decarboxylative N(1)-acylation of the carboxylic acid $1b$ with...
di-tert-butyl dicarbonate [20] and diazotization/bromination sequence. Reduction of N1-Boc protected dibromopyrazolotriazine 4 with further dehydrative aromatization of hydroxytriazine 5 in acidic media gave a mixture of compounds 3b and 3c in 57% overall yield. Formation of compound 3c can be explained in terms of electrophilic heteroaromatic ipso-substitution [26] of Br⁺ by H⁺. Crystals were successfully grown for all the isolated compounds and X-ray diffraction analyses were carried out.

Crystal structure discussion

Molecular structure description

Series of 7- or 8-monobromo compounds 2a,c and 3a,c are crystallized from ethyl acetate/dimethylsulfoxide (10:1) mixture in the monoclinic (the P2₁/c space group for 2a and P2₁/n for 3c), triclinic (the Pτ space group for 2c), and orthorhombic (Pnma for 3a) crystal systems without inclusion of solvent molecules into the crystal lattice. Compound 2d was simultaneously crystallized from ethyl acetate/DMSO (10:1) mixture at r.t. in two forms: as single crystals of non-solvated 7-bromo-3-tert-butyl-8-methylpyrazolo[5,1-c][1,2,4]triazine-4(1H)-one 2d in the orthorhombic crystal system (the Pnma space group), and as a 1:1 solvate with dimethylsulfoxide 2d·DMSO in the triclinic crystal system (the Pτ space group). 7,8-Dibromo pyrazolotriazines 2b and 3b were also crystalized from EtOAc/DMSO (10:1) mixture in the orthorhombic (Pnma) and monoclinic groups (P2₁/n) respectively. All studied crystal structures (Figs. 1, 2, and 3) exhibit similar geometries; yet, some subtle differences will be mentioned. Results of X-ray diffraction studies for compounds 2a-d and 3a-c are presented in Tables 3, 4, 5, and 6.

A slight increase in the C7–Br bond length compared to C8–Br for compounds 2c (1.854 (5) Å) and 2a (1.8658 (13) Å), respectively, is observed, which demonstrated the different π-electron density distribution in the conjugated system. The other bond distances are similar in both molecules. We were able to successfully switch the oxygen atom in 4-oxo derivative 2c to hydrogen and structurally characterize novel 7-bromo-3-tert-butylpyrazolo[5,1-c][1,2,4]triazine 3c as well. The latter compound was investigated by X-ray diffraction method, and it was found that, for 3c, the N1–N2, C3–C4, and N5–N6 bond lengths are shorter than the corresponding bonds in compounds 2a,c (Table 3), which indicate substantial increase in triazine ring conjugation for 3c compared to 2a and 2c. The Br atom in aromatic derivative 3c deviates more from the plane than in compounds 2a,c (~4° for 3c and ~2° for 2a,c), which can be explained by non-valence interactions, e.g., Br⋯N1 = 3.35 Å, H4⋯N1 = 2.35 Å (Table 6). The C–C bond lengths within the

| Bond | 2a | 2c | 3c |
|------|----|----|----|
| Br–C8 | 1.8658(13) | - | - |
| Br–C7 | - | 1.854(5) | 1.8619(11) |
| O–C4 | 1.2132(16) | 1.209(6) | - |
| N1–N2 | 1.3425(17) | 1.340(6) | 1.3153(13) |
| N1–C9 | 1.3478(18) | 1.351(6) | 1.3460(14) |
| N2–C3 | 1.3081(18) | 1.295(6) | 1.3668(13) |
| N5–C9 | 1.3670(17) | 1.378(6) | 1.3938(13) |
| N5–N6 | 1.3686(16) | 1.365(6) | 1.3492(13) |
| N5–C4 | 1.4011(18) | 1.387(7) | 1.3504(14) |
| N6–C7 | 1.3349(19) | 1.331(7) | 1.3523(14) |
| C3–C4 | 1.478(2) | 1.492(7) | 1.3788(15) |
| C7–C8 | 1.4035(19) | 1.410(7) | 1.3880(15) |
| C8–C9 | 1.380(2) | 1.390(7) | 1.3941(15) |

| Bond | 2d | 2d-DMSO | 3a |
|------|----|---------|----|
| Br–C7 | 1.8652(18) | 1.8670(8) | 1.8629(19) |
| O–C4 | 1.216(2) | 1.220(10) | - |
| C8–C14 | 1.495(3) | 1.495(3) | 1.499(3) |
| N1–N2 | 1.339(2) | 1.3335(10) | 1.308(2) |
| N1–C9 | 1.350(2) | 1.3521(10) | 1.354(2) |
| N2–C3 | 1.305(2) | 1.3076(10) | 1.381(3) |
| N5–N6 | 1.371(2) | 1.3620(10) | 1.345(2) |
| N5–C9 | 1.371(2) | 1.3751(9) | 1.384(2) |
| N5–C4 | 1.393(2) | 1.3928(11) | 1.360(2) |
| N6–C7 | 1.328(2) | 1.3284(11) | 1.350(2) |
| C3–C4 | 1.471(2) | 1.4694(11) | 1.366(3) |
| C7–C8 | 1.405(2) | 1.4070(11) | 1.388(3) |
| C8–C9 | 1.385(3) | 1.3828(11) | 1.398(3) |

| Bond | 2b | 3b |
|------|----|----|
| Br–C7 | 1.8569(17) | 1.851(7) |
| Br–C8 | 1.8576(16) | 1.855(6) |
| O–C4 | 1.213(2) | - |
| N1–N2 | 1.341(2) | 1.307(8) |
| N1–C9 | 1.345(2) | 1.349(9) |
| N2–C3 | 1.311(2) | 1.373(9) |
| N5–C9 | 1.365(2) | 1.382(9) |
| N5–N6 | 1.368(2) | 1.354(8) |
| N5–C4 | 1.402(2) | 1.368(8) |
| N6–C7 | 1.327(2) | 1.344(9) |
| C3–C4 | 1.471(2) | 1.384(9) |
| C7–C8 | 1.407(2) | 1.398(9) |
| C8–C9 | 1.380(2) | 1.387(9) |
1Bu group and distance C3–C10(Me3) vary from 1.522(2) Å to 1.549(9) Å for all compounds.

It is worth noting that the crystallization of 2d carried out under the same conditions gave two types of crystals—non-solvated and with inclusion of DMSO molecules into the crystal lattice. Both compounds have a similar structure, but the bromine atom in non-solvated 2d deviates more from the pyrazole plane (≈2° for 2d and ≈1° for 2d·DMSO), which can be explained by the large contribution of non-valent intermolecular interactions. The added methyl group at the C8 position and switching the oxygen atom to hydrogen at the C4 site was expected to change the molecular geometry—the Br–C7–C8–C9 torsion angle for 3a is 180.000(1)° compared to 3c (175.93(8)°). It is interesting to note that this angle remains practically unchanged for 4-oxopyrazolotriazines 3b and 3c (178.20(14)° and 178.2(4)°). Other torsion angles in compound 3a were approximately equal to 180°, which indicated a more pronounced aromatic character. The distances C8–C14 and C7–Br are similar for all compounds and vary from 1.489(3) Å to 1.4953(11) Å and from 1.8629(19) Å to 1.8670(8) Å, respectively.

Finally, the crystal structures of 7,8-dibromo-4-oxopyrazolo[5,1-c][1,2,4]triazine 2b and its 4-unsubstituted analog 3b were investigated. Both compounds readily produced single crystals and their structures were determined by X-ray diffraction. The C7–Br and C8–Br bond lengths in 7,8-dibromopyrazolo[5,1-c][1,2,4]triazines 2b and 3b have similar values which vary from 1.851(7) Å (C7–Br for 3b) to 1.8576(16) Å (C8–Br for 2b). The two bromine atoms in 2b deviate from the plane by ≈2°, while the corresponding atoms in 3b are held practically coplanar towards the whole bicyclic system. Similarly, the C10(Me3) moiety in 4-oxopyrazolotriazine 2b is located outside of the triazine ring (with a deviation of about 4°), while the corresponding atom in 4-unsubstituted analog 3b is located practically within the plane (N1–N2–C3–C10 = 179.9(6)°). The N1–N2, C3–C4, and N5–C4 bond lengths are significantly shorter in 3b compared to 2b, which proved the presence of a conjugated aromatic system in 3b.

### Non-valence interactions

The molecules form infinite 1D chains via hydrogen bonding along the c (2a) or b (2b, 2c, 2d·DMSO, 3c) axes: atom H1 interacts with both N6 and O1 atoms of a neighboring molecule (Figs. 1, 2, and 3). The experimental N1–H1 bond distances in all the studied compounds vary from 0.81(3) Å to 0.95Å (Table 6). It should be mentioned that these interactions are somewhat different among the studied crystals. Thus, the shortest donor···acceptor (D···A) distance and the largest D···A angle correspond to the bond N1–H1···O1 in 2d·DMSO, while the longest H-bond among the series was observed for compound 3c. On the contrary, C8–Me and C8–Br substituted analogs 3a,b do not tend to form any significant H-bonds. All the 4-oxo derivatives except for 2a (Fig. 1) exhibit two types of hydrogen bonds between N1H and N6 or O1 atoms. It is worth noting that both hydrogen bonds are nearly equal in 2b and 2d (Figs. 2 and 3 and Table 6).

C8–Br in compound 2a is coordinated with N5 and N2 atoms of the nearby molecules at nearly identical distances of 3.35–3.38Å. Similarly, C7–Br in compounds 2bd is coordinated with N2 (N2···Br = 3.41–3.42Å). However, bromine in a crystal lattice of analogous compound 2c with a vacant C8 position is surrounded by t-Bu groups and did not form any significant halogen bonds [27], apparently due to the competing H-bonding.

Molecules of compound 3c exhibited short contacts (N2···Br = 3.347(1)Å) which resemble that for 2b and 2d. An addition of C8–Me substituent to the aromatic pyrazolotriazine 3c led to considerable changes in the intermolecular interactions. Thus, every second molecule of 3a provided the bromine to form a pronounced halogen bond with the nearby azo-heterocycle (N6···Br = 3.014Å, Fig. 2). In compound 3b,
C8–Br and N6 atoms also form halogen bonds with the distance of 3.254(7) Å (Fig. 3).

Conclusions

To summarize, a total of eight isomeric pyrazole ring brominated 3-tert-butylypyrazolo[5,1-c][1,2,4]triazines have been for the first time investigated by X-ray single crystal diffraction analyses. Novel 7-bromo- and 7,8-dibromo-3-tert-butylypyrazolo[5,1-c][1,2,4]triazines were synthesized by reduction of triazine carbonyl with dehydrative aromatization in acidic media, and their XRD structural features were compared with that of the 4-oxo analogs. The experimental results revealed a marked increase in the aromatic character on switching oxygen atom in C4 position to hydrogen, which is indicated by the shortening of the heterocyclic bond lengths and smoothing of the torsion angles. Non-valence interactions and different packing modes depending upon the position of the bromine atoms were also considered.

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Author contribution The authors of the current manuscript Sergey M. Ivanov and Denis S. Koltun contributed equally to this work. All authors read and approved the final manuscript.

Data Availability The structures have been deposited at the Cambridge Crystallographic Data Center with the reference CCDC numbers 2065233-2065240; they also contain the supplementary crystallographic data. These data can be obtained free of charge from the CCDC via http://www.ccdc.cam.ac.uk/.

The online version of this article contains electronic supplementary material (ESM) on crystal structures, IR, NMR, and HRMS data for all new compounds.

Code availability Not applicable.

Declarations

Conflict of interest The authors declare no competing interests.

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