

3,6-Bis(2-pyridyl)di-1,2,4-triazolo-  
[3,4-a:4',3'-c]phthalazine

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The title compound,  $C_{20}H_{12}N_8$ , (I), has been prepared by the reaction of 1,4-dihydrazinophthalazine and pyridine-2-carboxaldehyde, followed by an oxidative cyclization by treatment with bromine. In the solid state, the molecules of (I) are discrete, comprising a fused and twisted four-ring system with an overall helical appearance. The distance between the two intramolecular pyridyl N atoms is 3.075 (2) Å, this short contact distance suggesting a  $\pi$ - $\pi$  interaction.

## Comment

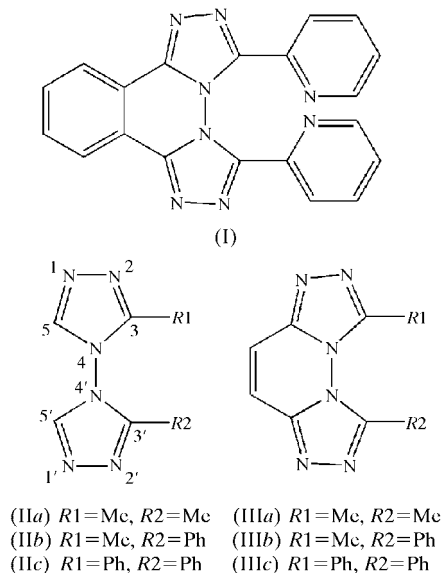
As a building block towards construction of polyheterocyclic ring systems of pharmaceutical interest, 1,4-dihydrazinophthalazine has attracted attention because it exhibits anti-hypertensive properties (Newkome & Paudler, 1982; Amer & Zimmer, 1983; Amer *et al.*, 1987). Many of its metabolites or derivatives are important because of their antibacterial and antitumor activities (Reece, 1981; Schneider *et al.*, 1988).

As a derivative of 1,4-dihydrazinophthalazine, the structure of the title compound, (I), is interesting because two triazole rings are fused to a parent phthalazine skeleton and two pendant pyridyl moieties are further connected to the triazole rings. If (I) is without a  $C_6$  ring, the remaining 4,4'-bis-1,2,4-triazole skeleton, (II) (see scheme), is that of a group of well known spin-crossover coordination complexes (Garcia *et al.*, 2001; Boillot *et al.*, 2002; Enachescu *et al.*, 2003).

A view of (I), with the atomic numbering scheme, is shown in Fig. 1, and selected geometric parameters are given in Table 1. Compound (I) is helical in that the two triazole rings are twisted in different directions, one up and one down, in relation to the similarly twisted plane of the fused four-ring system. The molecular symmetry of (I) in the crystalline state conforms to the chemical point group  $C_2$ . The bond lengths are in accordance with anticipated values (Orpen *et al.*, 1994).

The skeleton of (II) has two perpendicular triazole rings connected through an N-N bond (Domiano, 1977). Table 2 gives the  $C3-N4-N4'-C3'$  torsion angles for some 3,3'-disubstituted-4,4'-bis-1,2,4-triazoles (Sadybakasov, Sheinker, Struchkov, Shklover, Postovskii & Lundina, 1977; Carlsen *et al.*, 1992). This torsion angle is not  $90^\circ$  in molecules with 3,3'-

Me or Ph substituents; clearly, the torsion angle decreases with increasing size of the substituents. The nature of the driving force is believed to be electronically attractive rather than sterically repulsive, as illustrated by, for example,  $\pi$ - $\pi$  interactions (Sinnokrot *et al.*, 2002) in the case of 3-Ph,3'-Ph, (IIc).



When annealing with pyridazine or phthalazine, the constrained bis-1,2,4-triazole skeleton is expected to be planar. With substituents on the 3,3'-positions of the bis-1,2,4-triazole moiety, the  $C3-N4-N4'-C3'$  torsion angle deviates from  $0^\circ$  and increases with increasing steric bulkiness of the substituents [*e.g.* (IIIa) < (IIIb) < (IIIc)], as shown in Table 2 (Sadybakasov, Sheinker, Shklover *et al.*, 1977; Sadybakasov, Sheinker, Struchkov, Shklover, Timofeeva *et al.*, 1977; Sadybakasov, Timofeeva *et al.*, 1977). The  $C3-N4-N4'-C3'$  torsion angle is a convenient parameter for the measurement of planarity. This torsion angle in (I), having two pyridyl groups, corresponds well to that of (IIIc), having two phenyl groups. The deviation from planarity is attributed to the bulkiness of the substituents.

However, the shortest distance between the two pyridyl groups in (I) is that between atoms N22 and N32, which are only 3.075 (2) Å apart. As a pyridyl group is generally

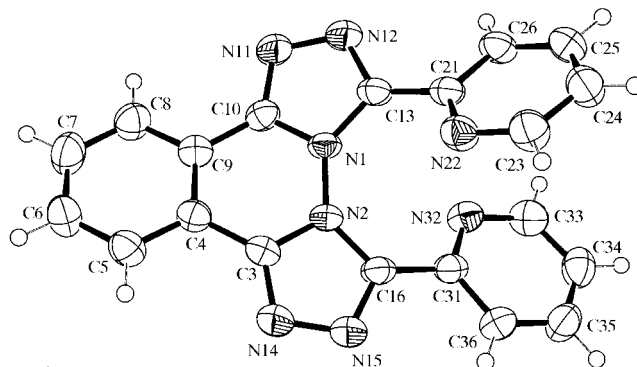


Figure 1

A view of (I), with the labelling of the non-H atoms. Displacement ellipsoids are shown at the 30% probability level.

regarded as a dipole and the two pyridyl rings in (I) are positioned with the two negative N atoms in close proximity, the short N...N contact is considered part of the more important, attractive,  $\pi$ - $\pi$  interactions rather than the negative dipole interactions. As a reference point, the shortest distance between the two phenyl rings in (IIIc) is 3.246 (2) Å, between the two *ipso*-C atoms. The distance between the two *ortho*-C atoms is 3.718 (2) Å.

The C-N bonds in bis-1,2,4-triazole are classified into localized single (e.g. N1-C10 and N1-C13) and double bonds (e.g. N11=C10 and N12=C13). The N1-C13 single bond is associated with a larger *endo* angle, N1-C13-C21, whereas the N12=C13 double bond has a smaller *exo* angle, N12=C13-C21.

The intermolecular short contacts are mostly due to C-H... $\pi$  or C-H...N interactions. Also notable are the  $\pi$ - $\pi$  interactions between two inversion-symmetry-related molecules [e.g. C10A...C10B = 3.362 (2) Å, C10A...N11B = 3.327 (2) Å and N11A...C10B = 3.327 (2) Å].

### Experimental

Compound (I) was prepared by the reaction of 1,4-dihydra-zinophthalazine with pyridine-2-carboxaldehyde, followed by an oxidative cyclization with bromine in the presence of acetic acid/sodium acetate buffer. The preparative method employed is an extension of a literature procedure (Pollak & Tisler, 1966). Single crystals suitable for X-ray structure determination were obtained from dichloromethane/hexane by slow evaporation.

#### Crystal data

C <sub>20</sub> H <sub>12</sub> N <sub>8</sub>	Mo K $\alpha$ radiation
<i>M<sub>r</sub></i> = 364.38	Cell parameters from 25 reflections
Monoclinic, <i>P</i> 2 <sub>1</sub> / <i>n</i>	$\theta$ = 5.8–18.5°
<i>a</i> = 8.1968 (12) Å	$\mu$ = 0.10 mm <sup>-1</sup>
<i>b</i> = 12.390 (2) Å	<i>T</i> = 293 (2) K
<i>c</i> = 16.409 (5) Å	Prism, light brown
$\beta$ = 91.23 (2)°	0.4 × 0.3 × 0.2 mm
<i>V</i> = 1666.1 (6) Å <sup>3</sup>	
<i>Z</i> = 4	
<i>D<sub>x</sub></i> = 1.453 Mg m <sup>-3</sup>	

#### Data collection

Enraf-Nonius CAD-4 diffractometer	<i>R</i> <sub>int</sub> = 0.018
Non-profiled $\omega/2\theta$ scans	$\theta$ <sub>max</sub> = 25.0°
Absorption correction: $\psi$ scan (North <i>et al.</i> , 1968)	<i>h</i> = 0 → 9
<i>T</i> <sub>min</sub> = 0.969, <i>T</i> <sub>max</sub> = 0.981	<i>k</i> = 0 → 14
3147 measured reflections	<i>l</i> = -19 → 19
2929 independent reflections	3 standard reflections
2101 reflections with <i>I</i> > 2 $\sigma$ ( <i>I</i> )	frequency: 60 min
	intensity decay: 1%

#### Refinement

Refinement on <i>F</i> <sup>2</sup>	$w = 1/[\sigma^2(F_o^2) + (0.04P)^2 + 0.3394P]$
$R[F^2 > 2\sigma(F^2)] = 0.033$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.095$	( $\Delta\rho$ ) <sub>max</sub> = 0.001
<i>S</i> = 1.02	$\Delta\rho$ <sub>max</sub> = 0.14 e Å <sup>-3</sup>
2929 reflections	$\Delta\rho$ <sub>min</sub> = -0.15 e Å <sup>-3</sup>
254 parameters	Extinction correction: <i>SHELXL97</i>
H-atom parameters constrained	Extinction coefficient: 0.0127 (13)

H atoms bonded to C atoms were treated as riding atoms (C-H = 0.93 Å).

Table 1

Selected geometric parameters (Å, °).

N1-C10	1.376 (2)	N22-C23	1.333 (2)
N1-C13	1.380 (2)	N22-C21	1.339 (2)
N1-N2	1.3857 (17)	N32-C31	1.337 (2)
N2-C3	1.376 (2)	N32-C33	1.339 (2)
N2-C16	1.382 (2)	C3-C4	1.446 (2)
N11-C10	1.312 (2)	C4-C9	1.400 (2)
N11-N12	1.385 (2)	C9-C10	1.446 (2)
N12-C13	1.314 (2)	C13-C21	1.461 (2)
N14-C3	1.308 (2)	C16-C31	1.465 (2)
N14-N15	1.377 (2)	N22-N32	3.075 (2)
N15-C16	1.313 (2)		
C10-N1-C13	106.46 (13)	N2-C3-C4	121.22 (14)
C10-N1-N2	119.52 (13)	C9-C4-C3	117.75 (15)
C13-N1-N2	133.95 (14)	C4-C9-C10	117.57 (15)
C3-N2-C16	106.07 (13)	N11-C10-N1	109.21 (15)
C3-N2-N1	118.75 (13)	N11-C10-C9	128.61 (16)
C16-N2-N1	135.17 (13)	N1-C10-C9	120.93 (14)
C10-N11-N12	107.22 (14)	N12-C13-N1	107.66 (15)
C13-N12-N11	109.27 (14)	N12-C13-C21	123.55 (15)
C3-N14-N15	107.13 (14)	N1-C13-C21	128.13 (14)
C16-N15-N14	109.65 (14)	N15-C16-N2	107.49 (15)
N14-C3-N2	109.51 (15)	N15-C16-C31	122.08 (15)
N14-C3-C4	128.35 (16)	N2-C16-C31	130.21 (14)
C10-N1-N2-C3	-22.1 (2)	N1-C13-C21-N22	-28.8 (3)
C10-N1-N2-C16	156.20 (17)	N1-C13-C21-C26	155.25 (17)
C13-N1-N2-C3	154.54 (17)	N12-C13-C21-N22	140.68 (17)
C13-N1-N2-C16	-27.2 (3)	N12-C13-C21-C26	-35.3 (3)
N2-N1-C13-N12	178.71 (15)	N2-C16-C31-N32	-18.1 (3)
N2-N1-C13-C21	-10.5 (3)	N2-C16-C31-C36	165.71 (17)
N1-N2-C16-N15	177.71 (15)	N15-C16-C31-N32	155.82 (16)
N1-N2-C16-C31	-7.7 (3)	N15-C16-C31-C36	-20.4 (3)

Table 2

The C3-N4-N4'-C3' torsion angle in (I), (II) and (III).

Compound	Torsion angle (°)	Substituents on R1 and R2
(I)†	27.2 (3)	Pyridine, pyridine
(II)‡	91.9 (5)	H, H
(IIa)§	84.1 (2)	Me, Me
(IIb)¶	74.3 (5)	Me, Ph
(IIc)§§	64.1 (2)	Ph, Ph
(IIIa)††	7.8 (5)	Me, Me
(IIIb)‡‡	20.7 (5)	Me, Ph
(IIIc)§§§	27.5 (5)	Ph, Ph

† This work. ‡ Domiano (1977). § Carlsen *et al.* (1992). ¶ Sadybakasov, Sheinker, Struchkov, Shklover, Postovskii & Lundina (1977). †† Sadybakasov, Sheinker, Shklover *et al.* (1977). ‡‡ Sadybakasov, Sheinker, Struchkov, Shklover, Timofeeva *et al.* (1977). §§ Sadybakasov, Timofeeva *et al.* (1977).

Data collection: *CAD-4 EXPRESS* (Enraf-Nonius, 1994); cell refinement: *CAD-4 EXPRESS*; data reduction: *XCAD4* (Harms & Wocadlo, 1995); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: TR1093). Services for accessing these data are described at the back of the journal.

## References

- Amer, A., Rashed, N., Rahman, M. M. A. & Zimmer, H. (1987). *Heterocycles*, **26**, 1277–1282.
- Amer, A. & Zimmer, H. (1983). *J. Heterocycl. Chem.* **20**, 1231–1238.
- Boillot, M.-L., Zarembowitch, J., Itié, J.-P., Polian, A., Bourdet, E. & Haasnoot, J. G. (2002). *New J. Chem.* pp. 313–322.
- Carlsen, P. H. J., Iversen, E. H., Samuelsen, E. J., Helgesson, G. & Jagner, S. (1992). *Acta Chem. Scand.* **46**, 200–204.
- Domiano, P. (1977). *Cryst. Struct. Commun.* **6**, 503–506.
- Enachescu, C., Linares, J., Codjovi, E., Boukheddaden, K. & Varret, F. (2003). *J. Optoelectr. Adv. Mater.* **5**, 261–266.
- Enraf–Nonius (1994). *CAD-4 EXPRESS*. Enraf–Nonius, Delft, The Netherlands.
- Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
- Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
- García, Y., Ksenofontov, V. & Gutlich, P. (2001). *C. R. Acad. Sci. Ser. IIC Chim.* **4**, 227–233.
- Harms, K. & Wocadlo, S. (1995). *XCAD4*. University of Marburg, Germany.
- Newkome, G. R. & Paudler, W. W. (1982). In *Contemporary Heterocyclic Chemistry: Syntheses, Reactions and Application*. New York: Wiley.
- North, A. C. T., Phillips, D. C. & Mathews, F. S. (1968). *Acta Cryst.* **A24**, 351–359.
- Orpen, A. G., Brammer, L., Allen, F. H., Kennard, O., Watson, D. G. & Taylor, R. (1994). *Structure Correlations*, Vol. 2, edited by H.-B. Bürgi & J. D. Dunitz, Appendix A. Weinheim, Germany: VCH Publishers.
- Pollak, A. & Tisler, M. (1966). *Tetrahedron*, **22**, 2073–2079.
- Reece, P. A. (1981). *Med. Res. Rev.* **1**, 73–96.
- Sadybakasov, B. K., Sheinker, Yu. N., Shklover, V. E., Struchkov, Yu. T., Lundina, I. B. & Postovskii, I. Ya. (1977). *Zh. Strukt. Khim.* **18**, 112.
- Sadybakasov, B. K., Sheinker, Yu. N., Struchkov, Yu. T., Shklover, V. E., Postovskii, I. Ya. & Lundina, I. B. (1977). *Zh. Strukt. Khim.* **18**, 1095.
- Sadybakasov, B. K., Sheinker, Yu. N., Struchkov, Yu. T., Shklover, V. E., Timofeeva, T. V., Postovskii, I. Ya. & Lundina, I. B. (1977). *Zh. Strukt. Khim.* **18**, 873.
- Sadybakasov, B. K., Timofeeva, T. V., Shklover, V. E., Struchkov, Yu. T., Postovskii, I. Ya., Lundina, I. B. & Sheinker, Yu. N. (1977). *Zh. Strukt. Khim.* **18**, 756.
- Schneider, T., Siegmund, W., Zschiesche, M., Kallwellis, R. & Scherber, A. (1988). *Pharmazie*, **43**, 33–36.
- Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
- Sinnokrot, M. O., Valeev, E. & Sherrill, C. D. (2002). *J. Am. Chem. Soc.* **124**, 10887–10893.