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1-[(2-Chlorophenyl)diphenylmethyl]-1*H*-pyrazole

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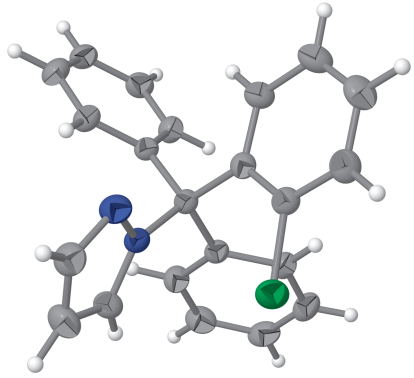
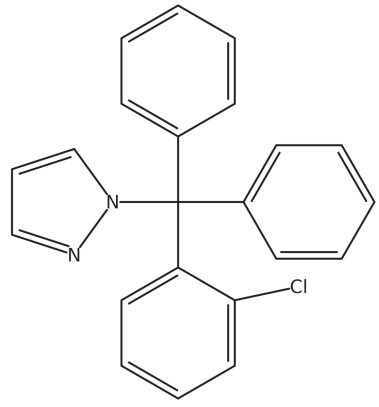
The title compound $C_{22}H_{17}ClN_2$, also named as TRAM-34, crystallizes in the monoclinic space group $P2_1/n$. The dihedral angles between the pyrazole ring and the three six-membered rings are 62.28 (9), 69.48 (9) and 71.30 (9)°.

3D view



Chemical scheme



Structure description

The title compound, $C_{22}H_{17}ClN_2$ (**I**) Fig. 1, also named as triarylmethane-34 (TRAM-34), is a structural isomer of the anti-fungal drug clotrimazole or 1-[(2-chlorophenyl)diphenylmethyl]-1*H*-imidazole. TRAM-34 is a selective and potent inhibitor of the intermediate-conductance, calcium-activated K^+ channels $K_{Ca}3.1$ (K_D = 20–25 n*M*) (Wulff *et al.*, 2000, 2001). TRAM-34 was synthesized and investigated in two studies to analyze the *in vivo* effect of combined irradiation and K_{Ca}-targeting with TRAM-34 in a glioma mouse model (Stransky *et al.*, 2023; Ganser *et al.*, 2024).

The dihedral angles in **I** between the pyrazole ring and the three six-membered rings (C7–C12, C13–C18, and C19–C24) are 62.28 (9), 69.48 (9), and 71.30 (9)°, respectively. The 2-chlorobenzene ring (C19–C24) is almost perpendicular to the C13–C18 ring [dihedral angle = 81.27 (7)°]. The dihedral angles between the C7–C12 ring and the C13–C18 and C19–C24 rings are 71.44 (8) and 69.05 (8)°, respectively. For the crystal structure of clotrimazole, see Song *et al.* (1998). In the extended structure of (**I**), some weak C—H$\cdots\pi$ interactions (Table 1) link the molecules Fig. 2.

Synthesis and crystallization

The title compound was prepared using the synthetic strategy reported by Wulff *et al.* (2000). To a suspension of 2-chlorotrityl chloride (12.5 g, 40 mmol) in acetonitrile (500 ml) was added pyrazole (8.17 g, 120 mmol). The reaction mixture was heated to reflux temperature for 3 h (during this time the reaction mixture became clear). After cooling to room temperature, the solvent was removed, and the residue was dissolved in ethyl acetate (200 ml). The organic phase was washed with water (3 × 150 ml). During

Table 1
Hydrogen-bond geometry (Å, °).

*Cg*2 and *Cg*3 are the centroids of the C7–C12 and C13–C18 rings, respectively.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C6—H6···*Cg*3^{i}	0.94	2.93	3.5594 (16)	125
C16—H16···*Cg*2^{ii}	0.94	2.88	3.6868 (18)	145
C20—H20···*Cg*3	0.94	2.89	3.6164 (17)	135

Symmetry codes: (i) $-x+1, -y+1, -z+1$; (ii) $x-1, y, z$.

this process, the title compound precipitated as a white solid, which was collected by filtration and dried (3.44 g, 25%). The filtrate was dried over sodium sulfate and solvent was evaporated. The obtained residue was recrystallized from hot ethanol solution to yield additional 7.11 g (52%) of the title compound as colorless crystals.

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2.

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{22}H_{17}ClN_2$
M_r	344.82
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	233
a, b, c (Å)	8.8768 (3), 18.3002 (7), 10.5053 (3)
β (°)	95.942 (3)
V (Å^3)	1697.39 (10)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.23
Crystal size (mm)	0.40 × 0.30 × 0.06
Data collection	
Diffractometer	Stoe IPDS 2T
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	22452, 4092, 2854
R_{int}	0.070
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.661
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.037, 0.089, 1.00
No. of reflections	4092
No. of parameters	226
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.25, −0.26

Computer programs: *X-AREA WinXpose*, *Recipe* and *Integrate* (Stoe & Cie, 2019), *SHELXT2014* (Sheldrick, 2015*a*), *SHELXL2018/3* (Sheldrick, 2015*b*) and *PLATON* (Spek, 2020).

References

Ganser, K., Stransky, N., Abed, T., Quintanilla–Martinez, L., Gonzalez–Menendez, I., Naumann, U., Koch, P., Krueger, M., Ruth, P., Huber, S. M. & Eckert, F. (2024). *Int. J. Cancre*, **155**, 1886–1901.

Sheldrick, G. M. (2015*a*). *Acta Cryst.* A**71**, 3–8.

Sheldrick, G. M. (2015*b*). *Acta Cryst.* C**71**, 3–8.

Song, H. & Shin, H.-S. (1998). *Acta Cryst.* C**54**, 1675–1677.

Spek, A. L. (2020). *Acta Cryst.* E**76**, 1–11.

Stoe & Cie (2019). *X-RED* and *X-AREA*. Stoe & Cie, Darmstadt, Germany.

Stransky, N., Ganser, K., Quintanilla-Martinez, L., Gonzalez-Menendez, I., Naumann, U., Eckert, F., Koch, P., Huber, S. M. & Ruth, P. (2023). *Sci. Rep.* **13**, 20604.

Wulff, H., Gutman, G. A., Cahalan, M. D. & Chandy, K. D. (2001). *J. Biol. Chem.* **276**, 32040–32045.

Wulff, H., Miller, M. J., Hänsel, W., Grissmer, S., Cahalan, M. D. & Chandy, K. D. (2000). *Proc. Natl Acad. Sci. USA*, **97**, 8151–8156.

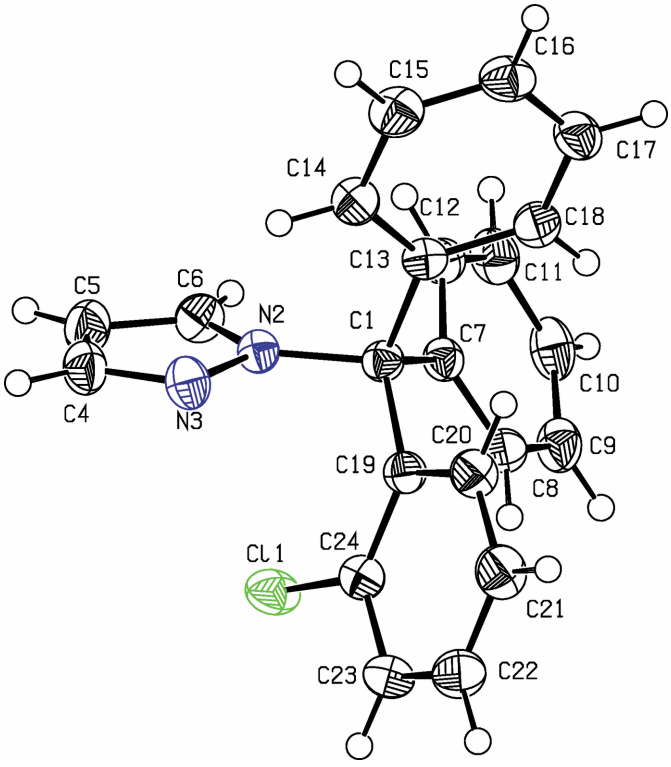


Figure 1
The molecular structure of **I**. Displacement ellipsoids are drawn at the 50% probability level.

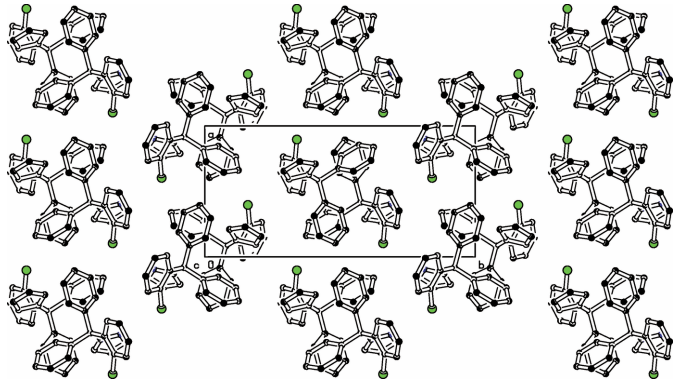


Figure 2
Part of the packing diagram viewed along the *c*-axis direction. Hydrogen atoms removed for clarity.