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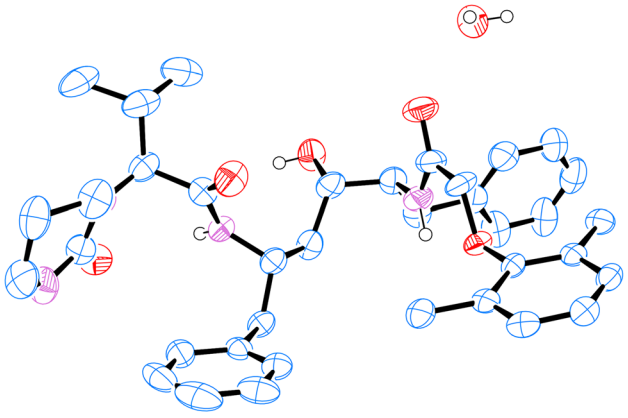
The crystal structure of N′-{5-[2-(2,6-dimethylphenoxy) acetamido]-4-hydroxy-1,6-diphenylhexan-2-yl}-3-methyl-2-(2-oxo-1,3-diazinan-1-yl)butanamide hydrate



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Abstract

$2(C_{37}H_{47}N_4O_5{\cdot}3(H_2O)$, triclinic, $P1$ (no. 1), a = 11.6319(7) Å, b = 13.9452(7) Å, c = 24.1727(14) Å, α = 106.203°, β = 103.296°, γ = 90.777°, V = 3651.7(4) Å^3, Z = 4, $R_{gt}(F)$ = 0.0682, w$R_{ref}(F^2)$ = 0.1899, T = 123 K.

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The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

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Table 1: Data collection and handling.

Crystal:	Colourless plate
Size:	0.34 × 0.09 × 0.03 mm
Wavelength:	CuKα radiation (1.54178 Å)
μ:	0.66 mm^{-1}
Diffractometer, scan mode:	Bruker D8 Venture photon, ω
θ_{max}, completeness:	65.0°, >99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	100,267, 24,878, 0.060
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 20,249
$N(param)_{refined}$:	1720
Programs:	Bruker [1], Shelx [2, 3], WinGX/Ortep [4], Mercury [5], Platon [6]

1 Source of materials

All reagents are commercially sourced without the need of further purifications. Approximately 0.010 g of lopinavir (0.0159 mmol) was dissolved in 5 mL of methanol. The solution was left in a polytop vial to allow slow evaporation at temperatures between 10 and 15 °C for 24 h. Colourless needles were formed and were observed after 5 weeks.

2 Experimental details

The collection method involved ω-scans of 0.5° width. The data was reduced using SAINT-Plus version 6.02.6 software. Sadabs was then used to process the empirical absorption corrections [1]. The crystal structure was solved using Shelxt [2]. Hydrogen atoms were geometrically positioned and U_{iso}(H) = 1.2U_{eq}(C). All diagrams were prepared for publication using Ortep [4], WinGX [4], Mercury [5] Platon [6].

3 Comment

Lopinavir is a selective and potent protease inhibitor used for the treatment and management of HIV infections [7]. Lopinavir was crystallised as a hydrate with methanol. The figure illustrates the asymmetric unit of the molecule, this unit consists of two molecules of N-{5-[2-(2,6-dimethylphenoxy)acetamido]-

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1A	−0.2574 (5)	0.0790 (4)	0.3976 (3)	0.0274 (13)
C2A	−0.2859 (6)	0.0726 (5)	0.3374 (3)	0.0340 (15)
C3A	−0.4043 (6)	0.0465 (5)	0.3063 (3)	0.0429 (17)
H3A	−0.426365	0.039566	0.264940	0.051*
C4A	−0.4886 (6)	0.0308 (5)	0.3346 (3)	0.0402 (17)
H4A	−0.568791	0.013306	0.312825	0.048*
C5A	−0.4588 (6)	0.0398 (5)	0.3935 (4)	0.0423 (17)
H5A	−0.518933	0.028435	0.412203	0.051*
C6A	−0.3418 (6)	0.0656 (5)	0.4277 (3)	0.0368 (15)
C7A	−0.3082 (8)	0.0779 (7)	0.4932 (4)	0.061 (2)
H7AA	−0.237636	0.042368	0.502759	0.091*
H7AB	−0.373840	0.050248	0.504738	0.091*
H7AC	−0.291061	0.149307	0.514924	0.091*
C8A	−0.1922 (7)	0.0921 (6)	0.3079 (3)	0.0475 (18)
H8AA	−0.163098	0.163064	0.323212	0.071*
H8AB	−0.225474	0.075001	0.264893	0.071*
H8AC	−0.126402	0.050881	0.316119	0.071*
C9A	−0.1001 (6)	0.1975 (5)	0.4615 (3)	0.0364 (15)
H9AA	−0.106526	0.207614	0.502845	0.044*
H9AB	−0.153813	0.241882	0.444312	0.044*
C10A	0.0267 (5)	0.2275 (5)	0.4623 (3)	0.0284 (13)
C11A	0.2089 (5)	0.1766 (5)	0.4320 (3)	0.0272 (13)
H11A	0.230445	0.250427	0.448590	0.033*
C12A	0.2895 (6)	0.1260 (5)	0.4728 (3)	0.0358 (15)
H12A	0.274184	0.052456	0.455183	0.043*
H12B	0.372873	0.144022	0.474117	0.043*
C13A	0.2748 (6)	0.1525 (5)	0.5352 (3)	0.0362 (15)
C14A	0.3441 (9)	0.2319 (6)	0.5796 (3)	0.057 (2)
H14A	0.402468	0.269728	0.570839	0.069*
C15A	0.3268 (13)	0.2554 (8)	0.6373 (4)	0.085 (4)
H15A	0.375064	0.308334	0.668014	0.102*
C16A	0.2426 (14)	0.2037 (11)	0.6493 (4)	0.091 (4)
H16A	0.229642	0.223273	0.688206	0.110*
C17A	0.1741 (10)	0.1231 (9)	0.6073 (4)	0.073 (3)
H17A	0.117508	0.085256	0.617226	0.088*
C18A	0.1905 (8)	0.0985 (7)	0.5489 (3)	0.052 (2)
H18A	0.143055	0.044247	0.518829	0.062*
C19A	0.2323 (5)	0.1441 (4)	0.3692 (2)	0.0242 (12)
H19A	0.314625	0.172209	0.373695	0.029*
C20A	0.1513 (5)	0.1875 (4)	0.3247 (2)	0.0251 (12)
H20A	0.068020	0.164896	0.320827	0.030*
H20B	0.159943	0.261522	0.340358	0.030*
C21A	0.1766 (5)	0.1577 (4)	0.2634 (2)	0.0246 (12)
H21A	0.177707	0.083184	0.249909	0.029*
C22A	0.2977 (5)	0.2058 (4)	0.2638 (2)	0.0257 (12)
H22A	0.294679	0.279456	0.274058	0.031*
H22B	0.359760	0.191008	0.295195	0.031*
C23A	0.3327 (5)	0.1698 (4)	0.2052 (3)	0.0254 (12)
C24A	0.3562 (5)	0.0697 (5)	0.1846 (3)	0.0306 (14)
H24A	0.346075	0.024393	0.206390	0.037*
C25A	0.3946 (6)	0.0356 (5)	0.1323 (3)	0.0321 (14)
H25A	0.411263	−0.032307	0.118752	0.038*
C26A	0.4081 (5)	0.1015 (5)	0.1005 (3)	0.0336 (15)
H26A	0.434222	0.078651	0.064942	0.040*
C27A	0.3842 (6)	0.1992 (5)	0.1196 (3)	0.0348 (15)
H27A	0.393023	0.243998	0.097331	0.042*
C28A	0.3465 (5)	0.2334 (5)	0.1727 (3)	0.0310 (14)
H28A	0.330416	0.301457	0.186054	0.037*
C29A	0.0134 (5)	0.1231 (5)	0.1741 (3)	0.0273 (13)
C30A	−0.0600 (5)	0.1681 (4)	0.1276 (2)	0.0263 (13)
H30A	−0.059042	0.241859	0.146225	0.032*
C31A	−0.1890 (5)	0.1243 (5)	0.1062 (3)	0.0301 (14)
H31A	−0.190827	0.050743	0.086684	0.036*
C32A	−0.2425 (7)	0.1396 (8)	0.1592 (4)	0.064 (3)
H32A	−0.196599	0.107033	0.187161	0.097*
H32B	−0.324666	0.110072	0.145792	0.097*
H32C	−0.240831	0.211432	0.178830	0.097*
C33A	−0.2594 (6)	0.1721 (5)	0.0615 (4)	0.0469 (19)
H33A	−0.258128	0.244311	0.080027	0.070*
H33B	−0.341475	0.142393	0.048205	0.070*
H33C	−0.224120	0.160452	0.027302	0.070*
C34A	0.0505 (5)	0.2321 (4)	0.0680 (3)	0.0279 (13)
C35A	−0.0092 (7)	0.0504 (5)	0.0376 (3)	0.0386 (16)
H35A	−0.082227	0.039490	0.005287	0.046*
H35B	−0.013974	0.000691	0.059514	0.046*
C36A	0.0956 (7)	0.0360 (5)	0.0120 (3)	0.0427 (17)
H36A	0.085940	−0.030748	−0.017606	0.051*
H36B	0.167571	0.038814	0.043803	0.051*
C37A	0.1101 (7)	0.1155 (5)	−0.0172 (3)	0.0429 (17)
H37A	0.188485	0.113498	−0.026746	0.052*
H37B	0.048320	0.102471	−0.054814	0.052*
N1A	0.0849 (4)	0.1591 (4)	0.4309 (2)	0.0269 (11)
H1A	0.046521	0.101336	0.408770	0.032*
N2A	0.0853 (4)	0.1878 (4)	0.2204 (2)	0.0246 (10)
H2A	0.077793	0.252146	0.225537	0.029*
N3A	−0.0008 (4)	0.1527 (3)	0.0784 (2)	0.0259 (11)
N4A	0.1004 (5)	0.2144 (4)	0.0217 (2)	0.0342 (12)
O1A	0.0686 (4)	0.3123 (3)	0.49173 (19)	0.0363 (10)
O2A	0.0052 (4)	0.0321 (3)	0.16678 (19)	0.0363 (11)
O3A	−0.1371 (4)	0.0970 (3)	0.42850 (18)	0.0295 (9)
O4A	0.2319 (4)	0.0391 (3)	0.34645 (18)	0.0283 (9)
H4AA	0.168678	0.011452	0.348090	0.043*
O5A	0.0499 (4)	0.3212 (3)	0.09908 (17)	0.0272 (9)
C1B	0.3082 (6)	0.7441 (5)	1.0764 (3)	0.0301 (14)
C2B	0.4222 (6)	0.7170 (5)	1.0929 (3)	0.0330 (14)
C3B	0.4768 (6)	0.7457 (5)	1.1535 (3)	0.0407 (16)
H3B	0.555765	0.730047	1.166654	0.049*
C4B	0.4173 (6)	0.7962 (5)	1.1942 (3)	0.0408 (16)
H4B	0.456835	0.816689	1.235136	0.049*
C5B	0.3025 (7)	0.8177 (5)	1.1772 (3)	0.0394 (16)
H5B	0.262439	0.850132	1.206458	0.047*
C7B	0.1194 (7)	0.8159 (6)	1.0970 (4)	0.0509 (19)
H7BA	0.119475	0.879269	1.086855	0.076*
H7BB	0.078760	0.821990	1.128924	0.076*
H7BC	0.078117	0.762079	1.061911	0.076*
C8B	0.4854 (6)	0.6578 (5)	1.0484 (3)	0.0417 (16)
H8BA	0.429848	0.634413	1.009295	0.063*
H8BB	0.516535	0.599983	1.060699	0.063*
H8BC	0.551078	0.700373	1.046360	0.063*
C9B	0.2809 (7)	0.7899 (6)	0.9882 (3)	0.0475 (18)
H9BA	0.368194	0.800942	0.996690	0.057*

Table 2: (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
H9BB	0.249710	0.854580	1.004784	0.057*
C10B	0.2311 (7)	0.7545 (6)	0.9232 (3)	0.0468 (18)
C11B	0.1049 (7)	0.6289 (6)	0.8387 (3)	0.0442 (17)
H11B	0.160028	0.649902	0.817150	0.053*
C12B	0.0968 (7)	0.5141 (6)	0.8225 (3)	0.0499 (19)
H12C	0.058406	0.493659	0.850449	0.060*
H12D	0.043769	0.487358	0.782278	0.060*
C13B	0.2102 (7)	0.4651 (6)	0.8230 (3)	0.0495 (19)
C14B	0.2052 (8)	0.3599 (7)	0.8122 (3)	0.061 (2)
H14B	0.131819	0.323687	0.806949	0.073*
C15B	0.3039 (9)	0.3101 (8)	0.8092 (4)	0.064 (2)
H15B	0.298340	0.239554	0.802510	0.077*
C16B	0.4096 (9)	0.3578 (8)	0.8155 (4)	0.069 (3)
H16B	0.477392	0.321372	0.812127	0.082*
C17B	0.4175 (10)	0.4599 (10)	0.8267 (6)	0.085 (3)
H17B	0.491732	0.495090	0.832360	0.102*
C18B	0.3183 (9)	0.5116 (8)	0.8299 (5)	0.070 (3)
H18B	0.325499	0.582183	0.837026	0.084*
C19B	−0.0131 (7)	0.6705 (6)	0.8206 (3)	0.0467 (18)
H19B	−0.001951	0.745235	0.836276	0.056*
C20B	−0.1117 (7)	0.6336 (6)	0.8435 (3)	0.0462 (18)
H20C	−0.079191	0.587802	0.866831	0.055*
H20D	−0.174424	0.594476	0.809022	0.055*
C21B	−0.1680 (6)	0.7167 (5)	0.8822 (3)	0.0405 (16)
H21B	−0.103062	0.760287	0.914432	0.049*
C22B	−0.2516 (7)	0.6738 (5)	0.9112 (3)	0.0406 (16)
H22C	−0.325726	0.644785	0.880762	0.049*
H22D	−0.214442	0.618518	0.925096	0.049*
C23B	−0.2830 (6)	0.7491 (5)	0.9632 (3)	0.0381 (16)
C24B	−0.2103 (7)	0.7690 (5)	1.0192 (3)	0.0433 (17)
H24B	−0.140422	0.734738	1.024693	0.052*
C25B	−0.2348 (8)	0.8366 (6)	1.0675 (4)	0.058 (2)
H25B	−0.182601	0.848499	1.105697	0.070*
C26B	−0.3348 (11)	0.8870 (7)	1.0604 (5)	0.073 (3)
H26B	−0.353153	0.933523	1.093650	0.088*
C27B	−0.4088 (9)	0.8692 (6)	1.0044 (6)	0.070 (3)
H27B	−0.477728	0.904655	0.999219	0.084*
C28B	−0.3840 (7)	0.8001 (6)	0.9553 (4)	0.055 (2)
H28B	−0.435732	0.788274	0.916986	0.066*
C29B	−0.2042 (6)	0.8771 (5)	0.8565 (3)	0.0421 (17)
C30B	−0.2894 (7)	0.9252 (6)	0.8160 (3)	0.0475 (18)
H30B	−0.328181	0.870438	0.779403	0.057*
C31B	−0.2242 (9)	1.0004 (7)	0.7964 (4)	0.064 (2)
H31B	−0.176332	1.051381	0.832646	0.077*
C32B	−0.1411 (10)	0.9486 (9)	0.7604 (5)	0.083 (3)
H32D	−0.078691	0.922368	0.785631	0.125*
H32E	−0.105175	0.996534	0.745079	0.125*
H32F	−0.185303	0.893232	0.727143	0.125*
C33B	−0.3147 (10)	1.0551 (8)	0.7606 (5)	0.076 (3)
H33D	−0.373821	1.005619	0.730218	0.114*
H33E	−0.273114	1.093013	0.741479	0.114*
H33F	−0.354283	1.101052	0.787551	0.114*
C34B	−0.4791 (7)	0.9062 (6)	0.8401 (3)	0.0481 (18)
C35B	−0.3505 (8)	1.0561 (6)	0.8964 (4)	0.061 (2)
H35C	−0.313657	1.037577	0.932761	0.073*
H35D	−0.292485	1.101429	0.889506	0.073*

Table 2: (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
C36B	−0.4580 (9)	1.1066 (7)	0.9036 (4)	0.067 (3)
H36C	−0.491437	1.127436	0.867652	0.081*
H36D	−0.436667	1.167801	0.937794	0.081*
C37B	−0.5500 (10)	1.0424 (7)	0.9134 (5)	0.071 (3)
H37C	−0.626985	1.072284	0.907613	0.085*
H37D	−0.527540	1.037690	0.954547	0.085*
C70C	0.2434 (6)	0.7924 (5)	1.1169 (3)	0.0363 (15)
N1B	0.1553 (6)	0.6732 (5)	0.9024 (3)	0.0466 (15)
H1B	0.134880	0.645389	0.927625	0.056*
N2B	−0.2297 (5)	0.7785 (4)	0.8470 (2)	0.0366 (13)
H2B	−0.289063	0.748556	0.816766	0.044*
N3B	−0.3835 (6)	0.9660 (4)	0.8454 (3)	0.0475 (15)
N4B	−0.5611 (7)	0.9405 (6)	0.8704 (3)	0.0607 (19)
O1B	0.2625 (5)	0.8017 (5)	0.8914 (3)	0.0655 (16)
O2B	−0.1199 (5)	0.9261 (4)	0.8957 (3)	0.0609 (15)
O3B	0.2506 (4)	0.7185 (3)	1.0160 (2)	0.0381 (11)
O4B	−0.0394 (5)	0.6433 (5)	0.7565 (2)	0.0567 (15)
H4BA	−0.111248	0.649602	0.743054	0.085*
O5B	−0.4959 (5)	0.8178 (4)	0.8054 (2)	0.0527 (13)
C1C	0.7794 (6)	0.3874 (4)	0.3873 (3)	0.0299 (14)
C2C	0.8495 (6)	0.4005 (4)	0.3502 (3)	0.0330 (14)
C3C	0.7957 (7)	0.3740 (5)	0.2896 (3)	0.0415 (17)
H3C	0.840774	0.380674	0.262508	0.050*
C4C	0.6777 (7)	0.3381 (6)	0.2683 (3)	0.0445 (18)
H4C	0.641237	0.323649	0.227101	0.053*
C5C	0.6132 (7)	0.3234 (5)	0.3066 (3)	0.0450 (18)
H5C	0.533063	0.296464	0.291164	0.054*
C6C	0.6620 (6)	0.3469 (5)	0.3674 (3)	0.0340 (15)
C7C	0.5926 (7)	0.3271 (6)	0.4081 (4)	0.0451 (17)
H7CA	0.552311	0.259451	0.391275	0.068*
H7CB	0.533522	0.376237	0.413001	0.068*
H7CC	0.646031	0.332469	0.446805	0.068*
C8C	0.9770 (7)	0.4403 (6)	0.3745 (4)	0.0488 (19)
H8CA	0.981812	0.509492	0.399764	0.073*
H8CB	1.013503	0.438829	0.341560	0.073*
H8CC	1.018892	0.398770	0.397956	0.073*
C9C	0.8040 (7)	0.5072 (5)	0.4805 (3)	0.0439 (17)
H9CA	0.716743	0.509046	0.472202	0.053*
H9CB	0.836589	0.560798	0.467476	0.053*
C10C	0.8542 (6)	0.5259 (5)	0.5465 (3)	0.0437 (17)
C11C	0.9874 (6)	0.4797 (6)	0.6266 (3)	0.0445 (18)
H11C	0.935433	0.519904	0.650371	0.053*
C12C	0.9984 (7)	0.3809 (6)	0.6422 (3)	0.0497 (19)
H12E	1.035503	0.334997	0.613367	0.060*
H12F	1.053719	0.394246	0.681870	0.060*
C13C	0.8871 (7)	0.3271 (7)	0.6434 (3)	0.050 (2)
C14C	0.8843 (9)	0.2249 (7)	0.6407 (4)	0.062 (2)
H14C	0.953199	0.190433	0.636708	0.075*
C15C	0.7865 (10)	0.1737 (9)	0.6437 (4)	0.072 (3)
H15C	0.788497	0.104817	0.641872	0.086*
C16C	0.6847 (10)	0.2207 (8)	0.6492 (4)	0.070 (3)
H16C	0.616200	0.185402	0.651364	0.084*
C17C	0.6851 (9)	0.3189 (9)	0.6515 (5)	0.075 (3)
H17C	0.614806	0.351845	0.654413	0.090*
C18C	0.7833 (8)	0.3723 (8)	0.6499 (4)	0.068 (2)
H18C	0.780462	0.441666	0.653190	0.082*

Table 2: (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
C19C	1.1020 (7)	0.5438 (6)	0.6402 (3)	0.0445 (18)
H19C	1.085048	0.602515	0.624398	0.053*
C20C	1.1991 (7)	0.4887 (6)	0.6140 (3)	0.0435 (17)
H20E	1.263156	0.480290	0.646797	0.052*
H20F	1.165437	0.420962	0.588367	0.052*
C21C	1.2528 (7)	0.5425 (5)	0.5774 (3)	0.0412 (16)
H21C	1.187492	0.550686	0.544442	0.049*
C22C	1.3448 (7)	0.4800 (5)	0.5497 (3)	0.0427 (17)
H22E	1.415691	0.481244	0.581825	0.051*
H22F	1.310906	0.409528	0.532155	0.051*
C23C	1.3827 (6)	0.5145 (5)	0.5031 (3)	0.0414 (17)
C24C	1.4825 (7)	0.5777 (6)	0.5168 (4)	0.0505 (19)
H24C	1.528579	0.599844	0.556678	0.061*
C25C	1.5172 (8)	0.6096 (7)	0.4740 (5)	0.060 (2)
H25C	1.585063	0.655752	0.484766	0.072*
C26C	1.4552 (9)	0.5757 (7)	0.4160 (5)	0.066 (3)
H26C	1.482771	0.594855	0.386247	0.080*
C27C	1.3503 (8)	0.5123 (7)	0.4003 (4)	0.060 (2)
H27C	1.304092	0.491321	0.360408	0.072*
C28C	1.3159 (7)	0.4813 (6)	0.4442 (3)	0.0428 (17)
H28C	1.246484	0.437200	0.434310	0.051*
C29C	1.2680 (8)	0.7282 (7)	0.6069 (4)	0.060 (2)
C30C	1.3423 (8)	0.8215 (6)	0.6525 (4)	0.057 (2)
H30C	1.386805	0.800296	0.687144	0.068*
C31C	1.2617 (10)	0.9014 (7)	0.6753 (5)	0.074 (3)
H31C	1.208379	0.916461	0.640425	0.088*
C32C	1.1843 (11)	0.8583 (9)	0.7086 (6)	0.093 (4)
H32G	1.137025	0.797639	0.681458	0.139*
H32H	1.131334	0.908298	0.722944	0.139*
H32I	1.235626	0.841884	0.742368	0.139*
C33C	1.3360 (12)	0.9981 (7)	0.7152 (5)	0.093 (4)
H33G	1.385861	0.985112	0.750544	0.139*
H33H	1.283206	1.049882	0.727307	0.139*
H33I	1.386383	1.021139	0.693271	0.139*
C34C	1.5372 (8)	0.8215 (6)	0.6331 (4)	0.055 (2)
C35C	1.3847 (10)	0.8933 (8)	0.5740 (5)	0.078 (3)
H35E	1.355085	0.837188	0.537434	0.093*
H35F	1.318365	0.935322	0.580674	0.093*
C36C	1.4831 (11)	0.9544 (9)	0.5666 (5)	0.087 (3)
H36E	1.454329	0.980197	0.532087	0.104*
H36F	1.509731	1.012538	0.602411	0.104*
C37C	1.5839 (11)	0.8935 (9)	0.5574 (5)	0.088 (4)
H37E	1.562506	0.843768	0.517664	0.105*
H37F	1.653345	0.937306	0.559416	0.105*
N1C	0.9280 (5)	0.4627 (4)	0.5635 (2)	0.0405 (14)
H1C	0.941901	0.409699	0.536798	0.049*
N2C	1.3069 (6)	0.6419 (4)	0.6138 (3)	0.0432 (14)
H2C	1.370275	0.645021	0.642484	0.052*
N3C	1.4271 (6)	0.8529 (5)	0.6256 (3)	0.0543 (17)
N4C	1.6133 (8)	0.8422 (6)	0.6032 (3)	0.074 (2)
O1C	0.8229 (5)	0.5992 (4)	0.5805 (2)	0.0593 (15)
O2C	1.1848 (8)	0.7356 (5)	0.5671 (4)	0.104 (3)
O3C	0.8330 (4)	0.4124 (3)	0.44826 (19)	0.0362 (10)
O4C	1.1479 (5)	0.5803 (4)	0.7040 (2)	0.0530 (14)
H4CA	1.098451	0.614936	0.719272	0.080*
O5C	1.5720 (6)	0.7737 (5)	0.6715 (3)	0.0666 (17)

Table 2: (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
C1D	1.3338 (5)	0.4176 (4)	0.0554 (3)	0.0287 (13)
C2D	1.3680 (5)	0.4683 (4)	0.1162 (3)	0.0296 (13)
C3D	1.4863 (6)	0.4685 (5)	0.1446 (3)	0.0387 (16)
H3D	1.512152	0.501745	0.185913	0.046*
C4D	1.5663 (6)	0.4224 (5)	0.1151 (4)	0.0416 (17)
H4D	1.646510	0.423357	0.135884	0.050*
C5D	1.5306 (6)	0.3742 (5)	0.0548 (3)	0.0411 (17)
H5D	1.587007	0.342511	0.034504	0.049*
C6D	1.4142 (6)	0.3713 (5)	0.0236 (3)	0.0342 (15)
C7D	1.3730 (8)	0.3212 (7)	−0.0423 (3)	0.056 (2)
H7DA	1.309147	0.269129	−0.049814	0.084*
H7DB	1.439356	0.290701	−0.057293	0.084*
H7DC	1.343610	0.371088	−0.062508	0.084*
C8D	1.2805 (7)	0.5202 (5)	0.1485 (3)	0.0412 (16)
H8DA	1.259557	0.580296	0.136256	0.062*
H8DB	1.315615	0.539375	0.191378	0.062*
H8DC	1.209033	0.474857	0.139013	0.062*
C9D	1.1822 (6)	0.4871 (5)	−0.0022 (3)	0.0334 (14)
H9DA	1.192424	0.464154	−0.043273	0.040*
H9DB	1.235749	0.548501	0.019276	0.040*
C10D	1.0563 (6)	0.5110 (4)	−0.0039 (3)	0.0302 (14)
C11D	0.8728 (5)	0.4805 (4)	0.0245 (3)	0.0267 (13)
H11D	0.849934	0.537552	0.007951	0.032*
C12D	0.7950 (6)	0.3863 (5)	−0.0175 (3)	0.0341 (14)
H12G	0.814016	0.329151	−0.001177	0.041*
H12H	0.710752	0.397606	−0.018607	0.041*
C13D	0.8104 (6)	0.3586 (5)	−0.0799 (3)	0.0327 (14)
C14D	0.8944 (7)	0.2937 (5)	−0.0962 (3)	0.0430 (17)
H14D	0.940703	0.265009	−0.068077	0.052*
C15D	0.9111 (7)	0.2706 (7)	−0.1534 (4)	0.056 (2)
H15D	0.967011	0.224618	−0.164554	0.067*
C16D	0.8462 (8)	0.3144 (7)	−0.1944 (3)	0.059 (2)
H16D	0.860013	0.300665	−0.232976	0.071*
C17D	0.7622 (8)	0.3776 (6)	−0.1788 (3)	0.056 (2)
H17D	0.716400	0.406693	−0.206900	0.067*
C18D	0.7443 (7)	0.3991 (5)	−0.1217 (3)	0.0441 (17)
H18D	0.685468	0.442526	−0.111309	0.053*
C19D	0.8487 (5)	0.5067 (4)	0.0864 (2)	0.0253 (12)
H19D	0.766623	0.529170	0.082087	0.030*
C20D	0.9306 (5)	0.5935 (4)	0.1316 (3)	0.0252 (12)
H20G	0.924515	0.652584	0.116365	0.030*
H20H	1.013455	0.575017	0.136018	0.030*
C21D	0.9027 (5)	0.6221 (4)	0.1927 (2)	0.0255 (12)
H21D	0.899401	0.559853	0.205343	0.031*
C22D	0.7848 (5)	0.6678 (4)	0.1930 (3)	0.0256 (12)
H22G	0.789095	0.731567	0.182807	0.031*
H22H	0.722180	0.621997	0.161484	0.031*
C23D	0.7488 (5)	0.6884 (4)	0.2507 (3)	0.0242 (12)
C24D	0.7258 (5)	0.6094 (5)	0.2727 (3)	0.0288 (13)
H24D	0.736248	0.543078	0.251349	0.035*
C25D	0.6885 (6)	0.6248 (5)	0.3245 (3)	0.0326 (14)
H25D	0.673616	0.569729	0.338538	0.039*
C26D	0.6729 (6)	0.7222 (5)	0.3561 (3)	0.0347 (15)
H26D	0.646326	0.734106	0.391594	0.042*
C28D	0.7346 (5)	0.7845 (5)	0.2839 (3)	0.0303 (14)
H28D	0.751838	0.839994	0.270733	0.036*

Table 2: (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
C29D	1.0635 (5)	0.6724 (4)	0.2841 (2)	0.0247 (13)
C30D	1.1398 (5)	0.7629 (4)	0.3312 (3)	0.0261 (13)
H30D	1.142096	0.818776	0.312994	0.031*
C31D	1.2671 (5)	0.7383 (5)	0.3529 (3)	0.0316 (14)
H31D	1.265673	0.684967	0.373115	0.038*
C32D	1.3199 (7)	0.6987 (9)	0.2997 (4)	0.067 (3)
H32J	1.278061	0.634008	0.275030	0.101*
H32K	1.404059	0.690003	0.313596	0.101*
H32L	1.311578	0.746421	0.276315	0.101*
C33D	1.3404 (7)	0.8310 (6)	0.3972 (4)	0.060 (2)
H33J	1.343021	0.883743	0.377750	0.089*
H33K	1.421213	0.814057	0.411470	0.089*
H33L	1.304229	0.854940	0.430841	0.089*
C34D	1.0301 (5)	0.8826 (4)	0.3895 (3)	0.0282 (13)
C35D	0.9622 (8)	0.8498 (6)	0.4735 (3)	0.0478 (18)
H35G	0.880796	0.852010	0.479441	0.057*
H35H	1.018273	0.878352	0.512695	0.057*
C36D	0.9854 (9)	0.7452 (7)	0.4483 (4)	0.059 (2)
H36G	1.001321	0.712624	0.480522	0.071*
H36H	0.912856	0.709902	0.418757	0.071*
C37D	1.0828 (8)	0.7324 (5)	0.4202 (3)	0.0457 (18)
H37G	1.080953	0.661052	0.397566	0.055*
H37H	1.158164	0.749826	0.451227	0.055*
27D	0.6965 (6)	0.8012 (5)	0.3351 (3)	0.0338 (14)
H	0.686248	0.867582	0.356393	0.041*
N1D	0.9975 (4)	0.4689 (4)	0.0259 (2)	0.0263 (11)
H1D	1.035946	0.432471	0.047358	0.032*
N2D	0.9958 (4)	0.6933 (3)	0.2370 (2)	0.0238 (10)
H2D	1.007533	0.752672	0.232296	0.029*
N3D	1.0797 (5)	0.7946 (4)	0.3798 (2)	0.0286 (11)
N4D	0.9751 (5)	0.9099 (4)	0.4346 (2)	0.0360 (13)
O1D	1.0139 (4)	0.5701 (3)	−0.03185 (19)	0.0356 (10)
O2D	1.0664 (4)	0.5882 (3)	0.29168 (19)	0.0357 (11)
O3D	1.2142 (4)	0.4110 (3)	0.02649 (18)	0.0295 (9)
O4D	0.8489 (4)	0.4217 (3)	0.10907 (18)	0.0273 (9)
H4DA	0.914633	0.397179	0.110306	0.041*
O5D	1.0327 (4)	0.9418 (3)	0.35767 (18)	0.0279 (9)
O1W	0.7402 (3)	0.6491 (3)	0.68525 (12)	0.0674 (17)
H1WA	0.682483	0.687704	0.682447	0.101*
H1WB	0.757366	0.649105	0.722242	0.101*
O2W	0.1105 (3)	0.3976 (3)	0.22708 (13)	0.0439 (12)
H2WA	0.047949	0.426775	0.234593	0.066*
H2WB	0.150262	0.392714	0.261220	0.066*
O3W	0.3960 (3)	0.6383 (3)	0.73942 (13)	0.0577 (14)
H3WA	0.406452	0.694676	0.767557	0.087*
H3WB	0.463689	0.612506	0.745386	0.087*
O4W	0.9770 (4)	0.8959 (3)	0.22969 (16)	0.0443 (12)
H4WA	1.003928	0.923905	0.206608	0.066*
H4WC	0.974716	0.917373	0.266398	0.066*
O5W	0.5974 (3)	0.5375 (3)	0.73680 (13)	0.191 (7)
H5WA	0.651735	0.572288	0.729206	0.287*
H5WB	0.521659	0.549227	0.725132	0.287*
O6W	0.8625 (3)	0.7908 (3)	0.58660 (12)	0.195 (7)
H6WA	0.855942	0.854965	0.598074	0.292*
H6WB	0.918164	0.784987	0.567433	0.292*

4-hydroxy-1,6-diphenylhexan-2-yl}-3-methyl-2-(2-oxo-1,3-diazinan-1-yl) butanamide and three molecules of water. All bond lengths and angles were as expected as reported by [8].

The secondary amine functional group is attached by a N2D–H2D···O4W bond to a water molecule, the bond length is recorded at 2.888 Å. Another secondary amine functional group is attached by a N2A–H2A···O2W bond to a water molecule with a bond length of 2.892 Å. The pyrimidinone moiety is attached by a C34–O5D···H4WC bond to a water molecule, the bond length was noted as 2.892 Å. These bond lengths are between 2.7 and 2.9 Å, according to [8] these bonds are considered moderate hydrogen bonds. Hydrates are crystal compounds that contain water in their crystal lattice [9]. The crystal structure synthesised is a hydrate, this is evident as there are three water molecules that interact with one another, but do not interact with the host molecule (lopinavir), making the crystal structure a trihydrate. The water molecules that interact with one another and those that interact with the host molecule are bifurcated hydrogen bond interactions. These water molecules are attached to one another by O5W–H5WB···O3W and O3W–H3WB···O5W bonds, both bond lengths 2.752 Å as well as O5W–H5WA···O1W bonds with a bond length of 2.949 Å.

Hydrates as well as cocrystals in general are found useful; they play a significant role in pharmaceutical drug design. These types of drugs are of key interest because water molecules are small and can form interactions as both hydrogen bond acceptors and donors. Hydrates are also considered non-toxic and are also able to form spontaneously [10].

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References

1. Bruker. *Apex3*, *Saint-Plus and Sadabs*; Bruker AXS Inc.: Madison, Wisconsin, USA, 2016.
2. Sheldrick G. M. Crystal structure refinement with SHELXL. *Acta Crystallogr.* 2015, *C71*, 3–8.
3. Sheldrick G. M. *SHELXL2018*; Universität Göttingen: Göttingen, Germany, 2018.
4. Farrugia L. J. WinGX and ORTEP for Windows: an update. *J. Appl. Crystallogr.* 2012, *45*, 849–854.
5. Macrae C. F., Edgington P. R., McCabe P., Pidcock E., Shields G. P., Taylor R., van der Streek T. Mercury 4.0: from visualization to

analysis, design and prediction. *J. Appl. Crystallogr.* 2020, *39*, 453–457.
6. Spek A. L. Structure validation in chemical crystallography. *Acta Crystallogr.* 2009, *D65*, 148–155.
7. Cvetkovic R. S., Goa K. L. Lopinavir/ritonavir – a review of its use in the management of HIV infection. *Drugs* 2003, *63*, 769–802.
8. Jeffrey G. A., *An Introduction to Hydrogen Bonding*; Oxford University Press: New York and Oxford, 1997. ISBN 0-19-509549-9.
9. Sanii R., Patyk-Kaźmierczak E., Hua C., Darwish S., Pham T., Forrest K. A., Space B., Zaworotko M. J. Toward an understanding of the propensity for crystalline hydrate formation by molecular compounds. Part 2. *Cryst. Growth Des.* 2021, *21*, 4927–4939.
10. Jurczak E., Mazurek A. H., Szeleszczuk Ł., Pisklak D. M., Zielińska-Pisklak M. Pharmaceutical hydrates analysis-overview of methods and recent advances. *Pharmaceutics* 2020, *12*, 959.