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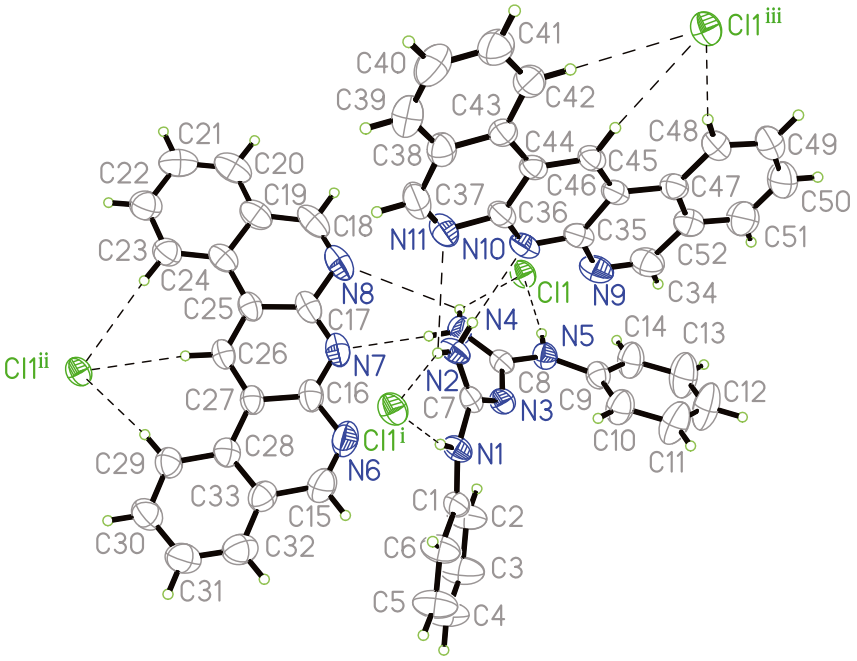
Crystal structure of *N*-((*Z*)-amino(((*E*)-amino(phenylamino)methylene) amino) methylene)benzenaminium chloride – benzo[*f*] isoquinolino[3,4-*b*][1,8]naphthyridine – tetrahydrofurane (1/2/2), $C_{60}H_{54}ClN_{11}O_2$



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Abstract

$C_{60}H_{54}ClN_{11}O_2$, $P\bar{1}$ (no. 2), a = 9.6795(10) Å, b = 14.8391(12) Å, c = 18.0298(14) Å, α = 90.710(3)°, β = 92.506(3)°, γ = 96.274(3)°, V = 2571.4(4) Å^3, Z = 2, $R_{gt}(F)$ = 0.0856, $wR_{ref}(F^2)$ = 0.2386, T = 296(2) K.

CCDC no.: 2183722.

Table 1: Data collection and handling.

Crystal:	Orange prism
Size:	0.20 × 0.20 × 0.10 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.13 mm^{-1}
Diffractometer, scan mode:	Bruker APEX3, φ and ω
θ_{max}, completeness:	30.6°, 99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	41,142, 15,536, 0.081
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 6655
$N(param)_{refined}$:	683
Programs:	Bruker [1], SHELX [2, 3]

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
Cl1	0.84264 (7)	0.62811 (5)	0.75706 (4)	0.0460 (2)
N1	0.1298 (3)	0.76108 (17)	0.78522 (13)	0.0400 (6)
H1N	0.048 (3)	0.733 (2)	0.7809 (16)	0.053 (10)*
N2	0.1876 (3)	0.62834 (18)	0.73783 (14)	0.0429 (6)
H2B	0.233 (3)	0.605 (2)	0.7084 (17)	0.049 (9)*
H2C	0.105 (4)	0.610 (2)	0.7382 (17)	0.051 (10)*
N3	0.3582 (2)	0.75290 (15)	0.75626 (12)	0.0402 (5)
N4	0.4797 (3)	0.63091 (18)	0.79316 (15)	0.0460 (6)
H4B	0.552 (4)	0.606 (2)	0.7967 (17)	0.055 (10)*
H4C	0.422 (3)	0.6104 (19)	0.8224 (16)	0.043 (9)*
N5	0.5854 (3)	0.74384 (17)	0.72597 (13)	0.0408 (6)
H5N	0.648 (3)	0.7145 (19)	0.7293 (16)	0.042 (9)*
N6	0.2106 (3)	0.67792 (19)	0.94614 (15)	0.0663 (8)
N7	0.3222 (3)	0.55316 (19)	0.92495 (13)	0.0539 (7)
N8	0.4441 (3)	0.4353 (2)	0.89442 (15)	0.0663 (8)
N9	0.4405 (3)	0.63848 (18)	0.56850 (14)	0.0546 (7)
N10	0.2579 (3)	0.53717 (16)	0.59974 (12)	0.0445 (6)
N11	0.0755 (3)	0.44527 (19)	0.64271 (13)	0.0549 (7)
C1	0.1418 (3)	0.84160 (19)	0.82797 (15)	0.0413 (7)
C2	0.2646 (4)	0.8851 (2)	0.8580 (2)	0.0628 (9)
H2A	0.348626	0.863166	0.848669	0.075*
C3	0.2625 (5)	0.9617 (3)	0.9023 (2)	0.0803 (12)
H3A	0.346038	0.991167	0.922008	0.096*
C4	0.1413 (5)	0.9952 (3)	0.9176 (2)	0.0843 (13)
H4A	0.141712	1.046815	0.947412	0.101*
C5	0.0190 (5)	0.9515 (3)	0.8886 (2)	0.0840 (13)
H5A	−0.064676	0.973114	0.899206	0.101*
C6	0.0186 (4)	0.8756 (2)	0.8435 (2)	0.0638 (9)
H6A	−0.065328	0.847079	0.823433	0.077*
C7	0.2301 (3)	0.71271 (18)	0.76098 (13)	0.0362 (6)
C8	0.4691 (3)	0.70751 (18)	0.75753 (14)	0.0369 (6)
C9	0.6074 (3)	0.81463 (19)	0.67556 (15)	0.0419 (7)
C10	0.5054 (4)	0.8643 (2)	0.64642 (19)	0.0603 (9)
H10A	0.414133	0.852538	0.660677	0.072*
C11	0.5404 (5)	0.9313 (3)	0.5960 (2)	0.0830 (12)
H11A	0.472070	0.965192	0.577067	0.100*
C12	0.6738 (5)	0.9488 (3)	0.5735 (3)	0.0934 (14)
H12A	0.695621	0.993874	0.539194	0.112*
C13	0.7744 (5)	0.8995 (3)	0.6017 (2)	0.0877 (13)
H13A	0.865082	0.910694	0.586336	0.105*
C14	0.7417 (4)	0.8332 (2)	0.65279 (19)	0.0616 (9)
H14A	0.811115	0.800426	0.672229	0.074*
C15	0.1286 (4)	0.7193 (2)	0.9854 (2)	0.0704 (11)
H15A	0.112513	0.777245	0.970685	0.084*
C16	0.2365 (3)	0.5924 (2)	0.96797 (15)	0.0497 (8)
C17	0.3535 (3)	0.4703 (2)	0.94175 (16)	0.0505 (8)
C18	0.4764 (4)	0.3553 (3)	0.90744 (19)	0.0694 (10)
H18A	0.537603	0.332514	0.875533	0.083*
C19	0.4278 (3)	0.2969 (2)	0.96631 (17)	0.0564 (8)
C20	0.4686 (4)	0.2103 (3)	0.9752 (2)	0.0723 (11)
H20A	0.529989	0.189016	0.942648	0.087*
C21	0.4193 (4)	0.1563 (3)	1.0313 (2)	0.0705 (10)
H21A	0.444861	0.097978	1.036312	0.085*
C22	0.3304 (4)	0.1899 (2)	1.08065 (19)	0.0633 (9)
H22A	0.298405	0.154107	1.119668	0.076*
C23	0.2891 (4)	0.2745 (2)	1.07293 (17)	0.0541 (8)
H23A	0.228147	0.295068	1.106115	0.065*
C24	0.3373 (3)	0.3303 (2)	1.01572 (15)	0.0457 (7)
C25	0.2988 (3)	0.4208 (2)	1.00322 (14)	0.0422 (7)
C26	0.2112 (3)	0.4637 (2)	1.04717 (14)	0.0435 (7)
H26A	0.174330	0.434025	1.088214	0.052*
C27	0.1774 (3)	0.54951 (19)	1.03123 (14)	0.0414 (7)
C28	0.0851 (3)	0.59818 (19)	1.07370 (15)	0.0433 (7)
C29	0.0166 (3)	0.5638 (2)	1.13616 (16)	0.0523 (8)
H29A	0.032053	0.506809	1.153408	0.063*
C30	−0.0727 (4)	0.6133 (2)	1.17203 (18)	0.0608 (9)
H30A	−0.117802	0.589495	1.213102	0.073*
C31	−0.0961 (4)	0.6992 (2)	1.14713 (19)	0.0663 (10)
H31A	−0.156808	0.732387	1.171691	0.080*
C32	−0.0311 (4)	0.7343 (2)	1.08754 (19)	0.0657 (10)
H32A	−0.046795	0.791824	1.071629	0.079*
C33	0.0597 (4)	0.6848 (2)	1.04940 (16)	0.0519 (8)
C34	0.5200 (4)	0.6734 (2)	0.51832 (18)	0.0568 (8)
H34A	0.587601	0.720183	0.533328	0.068*
C35	0.3393 (3)	0.56916 (19)	0.54623 (15)	0.0421 (7)
C36	0.1572 (3)	0.4708 (2)	0.58368 (14)	0.0420 (7)
C37	−0.0231 (4)	0.3810 (2)	0.63096 (17)	0.0590 (9)
H37A	−0.078014	0.364880	0.670781	0.071*
C38	−0.0575 (3)	0.3312 (2)	0.56224 (16)	0.0488 (7)
C39	−0.1662 (4)	0.2616 (2)	0.5546 (2)	0.0642 (9)
H39A	−0.219080	0.245937	0.595268	0.077*
C40	−0.1966 (4)	0.2161 (2)	0.4889 (2)	0.0717 (11)
H40A	−0.269932	0.170013	0.484523	0.086*
C41	−0.1161 (4)	0.2395 (2)	0.4279 (2)	0.0657 (10)
H41A	−0.134883	0.207744	0.383177	0.079*
C42	−0.0104 (4)	0.3083 (2)	0.43350 (17)	0.0528 (8)
H42A	0.040473	0.323802	0.392076	0.063*
C43	0.0230 (3)	0.35629 (18)	0.50097 (15)	0.0413 (7)
C44	0.1328 (3)	0.42902 (18)	0.51176 (14)	0.0370 (6)
C45	0.2181 (3)	0.46372 (18)	0.45685 (14)	0.0394 (6)
H45A	0.205377	0.439093	0.409036	0.047*
C46	0.3216 (3)	0.53412 (18)	0.47161 (14)	0.0392 (6)
C47	0.4129 (3)	0.57585 (19)	0.41702 (15)	0.0439 (7)
C48	0.4064 (4)	0.5487 (2)	0.34172 (16)	0.0570 (9)
H48A	0.340018	0.502365	0.324331	0.068*
C49	0.4984 (4)	0.5910 (2)	0.29414 (19)	0.0712 (11)
H49A	0.493804	0.572582	0.244525	0.085*
C50	0.5984 (4)	0.6609 (3)	0.3184 (2)	0.0740 (11)
H50A	0.660367	0.688632	0.285456	0.089*
C51	0.6046 (4)	0.6883 (2)	0.3911 (2)	0.0680 (10)
H51A	0.670467	0.735485	0.407478	0.082*
C52	0.5133 (3)	0.6463 (2)	0.44113 (17)	0.0499 (7)
O1[a]	0.8600 (8)	0.9901 (5)	0.4013 (4)	0.121 (3)*
C53[a]	0.776 (2)	0.9786 (12)	0.3276 (8)	0.203 (7)*
H53A[a]	0.677453	0.969956	0.337297	0.243*
H53B[a]	0.792830	1.033435	0.299177	0.243*
C54[a]	0.8103 (16)	0.9037 (8)	0.2852 (6)	0.149 (4)*
H54A[a]	0.725995	0.865788	0.269080	0.179*
H54B[a]	0.857483	0.925262	0.241376	0.179*
C55[a]	0.8978 (13)	0.8523 (7)	0.3286 (5)	0.111 (3)*
H55A[a]	0.985218	0.848284	0.305096	0.133*
H55B[a]	0.853049	0.791455	0.335726	0.133*
C56[a]	0.920 (2)	0.9004 (10)	0.3974 (8)	0.162 (7)*
H56A[a]	1.019465	0.911270	0.408520	0.195*
H56B[a]	0.880392	0.861948	0.435987	0.195*

Table 2: (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
O1A[b]	0.8489 (16)	1.0102 (8)	0.3281 (7)	0.154 (6)*
C53A[b]	0.899 (2)	0.9330 (11)	0.2862 (7)	0.119 (6)*
H53C[b]	0.822799	0.896754	0.259719	0.143*
H53D[b]	0.967856	0.954870	0.251082	0.143*
C54A[b]	0.9607 (19)	0.8814 (11)	0.3443 (8)	0.105 (5)*
H54C[b]	1.061262	0.894439	0.346601	0.126*
H54D[b]	0.936858	0.816877	0.335363	0.126*
C55A[b]	0.901 (2)	0.9105 (14)	0.4155 (8)	0.117 (7)*
H55C[b]	0.874376	0.858908	0.446130	0.141*
H55D[b]	0.967498	0.953159	0.443577	0.141*
C56A[b]	0.786 (2)	0.9516 (14)	0.3899 (11)	0.153 (7)*
H56C[b]	0.751199	0.988164	0.428441	0.184*
H56D[b]	0.711436	0.907224	0.370705	0.184*
O2[c]	0.3367 (10)	0.9454 (6)	0.1448 (4)	0.148 (3)*
C57[c]	0.4119 (19)	0.9521 (10)	0.2184 (9)	0.200 (7)*
H57A[c]	0.510958	0.954579	0.211308	0.240*
H57B[c]	0.395070	1.008199	0.242866	0.240*
C58[c]	0.3699 (18)	0.8753 (11)	0.2674 (7)	0.193 (6)*
H58A[c]	0.319176	0.894256	0.309020	0.231*
H58B[c]	0.449332	0.846135	0.285613	0.231*
C59[c]	0.2763 (16)	0.8143 (8)	0.2126 (7)	0.148 (5)*
H59A[c]	0.323476	0.764040	0.195530	0.178*
H59B[c]	0.190845	0.790622	0.235067	0.178*
C60[c]	0.2500 (12)	0.8715 (7)	0.1550 (6)	0.144 (4)*
H60A[c]	0.243875	0.835788	0.109385	0.172*
H60D[c]	0.158603	0.890806	0.161577	0.172*
O2A[d]	0.349 (2)	0.8073 (12)	0.2464 (12)	0.233 (8)*
C57A[d]	0.4670 (18)	0.8702 (14)	0.2211 (12)	0.177 (8)*
H57C[d]	0.514391	0.903178	0.263318	0.212*
H57D[d]	0.533198	0.836123	0.197210	0.212*
C58A[d]	0.414 (3)	0.9333 (16)	0.1691 (14)	0.202 (11)*
H58C[d]	0.387354	0.905034	0.120962	0.242*
H58D[d]	0.479010	0.986740	0.163096	0.242*
C59A[d]	0.289 (2)	0.9541 (12)	0.2105 (12)	0.172 (8)*
H59C[d]	0.314680	1.001042	0.248053	0.206*
H59D[d]	0.217470	0.973568	0.176886	0.206*
C60A[d]	0.245 (2)	0.8729 (17)	0.2423 (17)	0.229 (12)*
H60B[d]	0.162912	0.845287	0.214087	0.275*
H60C[d]	0.216803	0.884981	0.292167	0.275*

[a]Occupancy: 0.609 (12). [b]Occupancy: 0.391 (12). [c]Occupancy: 0.599 (9). [d]Occupancy: 0.401 (9).

The molecular structure is shown in the figure (symmetry code i) $x-1, y, z$; ii) $-x+1, -y+1, -z+2$; iii) $-x+1, -y+1, -z+1$). The disordered THF molecule is not shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of material

N-((*Z*)-amino(((*E*)-amino(phenylamino)methylene)amino) methylene)benzenaminium chloride (diphenylbiguanide chloride, HL^+Cl^-) and benzo[*f*]isoquinolino[3,4-*b*][1,8] naphthyridine (anthiridine, DBA) was synthesized by following the literature procedures [4, 5]. The title compound, i.e., the cocrystal of between HL^+Cl^- and DBA was prepared by dissolving the two compounds in THF solution in a molar ratio of 1:2. The solution was filtered to obtain a yellow clear filtrate, which was kept in a glass vial sealed with parafilm. Prism crystals with orange color were obtained with a few days.

Experimental details

A crystal of a size 0.20 × 0.20 × 0.10 mm was mounted on a glass fiber with expoxy glue. Data collection was performed on a Bruker D8 VENTURE Photon II diffractometer. Data were processed on a PC using the Bruker AXS Crystal Structure Analysis Package [1]. Data collection: Bruker APEX3; cell refinement: Bruker SAINT; Data reduction: Bruker SAINT; Structure solution: SHELXT 2014/5 [2]; Structure refinement: SHELXL-2018/3 [3]; Molecular graphics: Bruker SHELXTL [2]; Publication materials: Bruker SHELXTL [2].

The H-atoms on N-atoms were located from the difference-Fourier maps, and refined without any constraints. All other H-atoms were placed geometrically and refined using a riding model with common isotropic displacement factors $U_{iso}(H) = 1.2\ U_{eq}$(parent C-atom). The two THF molecules were disordered.

Comment

The simplest biguanide, 2-carbamimidoylguanidine, was synthesized by Rathke in 1879 [6]. 50 years later, some biguanide derivatives, including metformin (3-(diaminomethylene)-1,1-dimethylguanidine) were found to be able to lower the blood glucose in animals [7, 8]. However, due to their side effects and the availability of insulin, metformin did not receive too much attention until its introduction into USA by FDA in 1995 [9]. Currently, metformin is the first-line therapy for treatment of type 2 diabetes. In addition, metformin and its analogues have found a variety of therapeutic applications, such as, polycystic ovary syndrome [10], cardiovascular disease [11], anti-aging [12] and even COVID-19 [13]. Meanwhile, biguanides also have demonstrated potential applications in the development of highly efficient solar cells recently, due to its capability for hydrogen bonding formation [14, 15].

Crystal engineering is the science to build crystalline materials of specific characteristics or physicochemical

properties through intermolecular interactions. Hydrogen bonding, especially multi-hydrogen bonding, is very important for crystal engineering and plays important roles on structure stability, directionality and physicochemical properties [16–18].

With a structure characterized with multiple –NH, it is reasonable to assume that HL^+Cl^- can behave as an multi-hydrogen bond donor, which can form multi-hydrogen bonds with hydrogen bond acceptors to form multi-hydrogen bond pairs, such as DD…AA or DDD…AAA. DBA, as we can see from its structure, is a planar hydrogen bond acceptor, *i.e.*, AAA. We have found that the packing of DBA molecules in a crystal can be tuned through crystal engineering, which alters the way of the π–π stacking of the DBA molecules and leads to the change of electro-conductivity of the crystals. Here we report the structure of a novel co-crystal between HL^+Cl^- and two DBA, with the one HL^+ hydrogen bonded to two DBA through two sets of DD···AA and each Cl^- is hydrogen bonded to two DBA through two triple C–H···Cl^- hydrogen bonds and to two HL^+ through two double N–H···Cl^- hydrogen bonds. All nitrogen containing species are connected to each other or form a hydrogen bond to the chloride anion. The disordered THF molecules fill the gaps between the hydrogen bonded molecules and ions. Bond lengths are all in the expected ranges [19, 20].

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

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Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

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