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(+*ac*,−*ac*)-*trans*-Bis(hinokitiolato)-copper(II) and its chloroform disolvate

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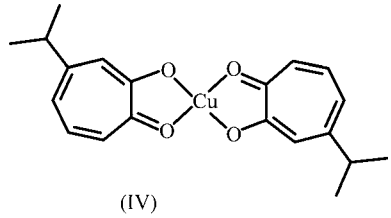
The complex *trans*-bis(hinokitiolato)copper(II) [systematic name: *trans*-bis(3-isopropyl-7-oxocyclohepta-1,3,5-trienolato)-copper(II); abbreviated name: *trans*-Cu(hino)$_2$], [Cu-($C_{10}H_{11}O_2$)$_2$], is a biologically active compound. Three polymorphs of this square-planar monomer, all with (+*sp*,−*sp*) isopropyl substituents, have been reported previously. A fourth polymorph containing (+*ac*,−*ac*) isopropyl groups and its chloroform disolvate, [Cu($C_{10}H_{11}O_2$)$_2$]·2$CHCl_3$, both exhibiting nonmerohedral twinning and with all Cu atoms on centers of crystallographic inversion symmetry, are reported here. One of the differences between all of these polymorphs is the relative conformation of the isopropyl groups with respect to the plane of the molecule. Stacking and Cu···olefin π distances ranging from 3.214 (4) to 3.311 (2) Å are observed, and the chloroform solvent molecules participate in bifurcated C—H···O hydrogen bonds [H···O = 2.26–2.40 Å, C···O = 3.123 (5)–3.214 (5) Å, C—H···O = 127–151° and O···H···O = 74°].

Comment

Hinokitiol (β-thujaplicin), a natural product first isolated from *Chamaecyparis taiwanensis* (Nozoe, 1936), is a tropolone possessing antimicrobial activity. Its antibacterial and antifungal properties have contributed to its widespread utilization in agricultural and personal care products. Not surprisingly, it is also an excellent ligand for the chelation of metal ions. Hence, metal hinokitiolate complexes, *M*(hino)$_x$, have also attracted renewed interest and scrutiny. For example, Cu, Zn and Sn hinokitiolate complexes have been examined for their suitability in oral care products (Creeth *et al.*, 2000), one polymorph of *trans*-Cu(hino)$_2$ has been shown to possess antibacterial properties (Nomiya, Yoshizawa, Tsukagoshi *et al.*, 2004; Nomiya, Yoshizawa, Kasuga *et al.*, 2004), and Cu(hino)$_2$ has been reported to inhibit the replication of human influenza viruses (Miyamoto *et al.*, 1998). In the last example, our use of Cu(hino)$_2$ without qualifications is to specify that, to our knowledge, the identity of the compound in that study is not known with certainty.

Antibacterial studies involving Cu indicate a growing need for more precise language and nomenclature in the discussion of these compounds. The reader is cautioned that Cu(hino)$_2$ as written does not imply a single compound. Rather, Cu(hino)$_2$ is shorthand for a family of compounds. The members of that family include *cis*-Cu(hino)$_2$, *trans*-Cu(hino)$_2$, and any combination of monomers, dimers and/or oligomers with the empirical formulation Cu(hino)$_2$. Molloy and co-workers were the first to 'report on the unusual structural chemistry' of Cu(hino)$_2$ (Barret *et al.*, 2002). The *cis* monomer has yet to be isolated in pure form, the *trans* monomer is polymorphic, and a third family member, [*cis*-Cu(hino)$_2$]$_2$·[*trans*-Cu(hino)$_2$]$_2$·-*trans*-Cu(hino)$_2$, has been confirmed. This last was used as the starting material for this study.



(IV)
(V) = (IV)·2$CHCl_3$

It is also important to clarify that the 1:1:1 combination of the *cis*-dimer, *trans*-dimer and *trans*-monomer has never been shown to pack in any arrangement other than that reported in 2002, and hence cannot be said to be polymorphic. Further, it is not a polymorph of the *cis*- or *trans*-monomeric members of the family. To transform one family member into another requires geometric isomerization and/or covalent bond breaking and bond making, and as such they are not polymorphs of each other according to the most widely accepted definition of polymorphism (McCrone, 1965). These polymers (dimers, oligomers, *etc.*) and dynamic isomers (as stated by McCrone) 'cannot be called polymorphs although they may behave in a confusingly similar manner'. Currently, only one member within the Cu(hino)$_2$ family of compounds, *viz.* *trans*-

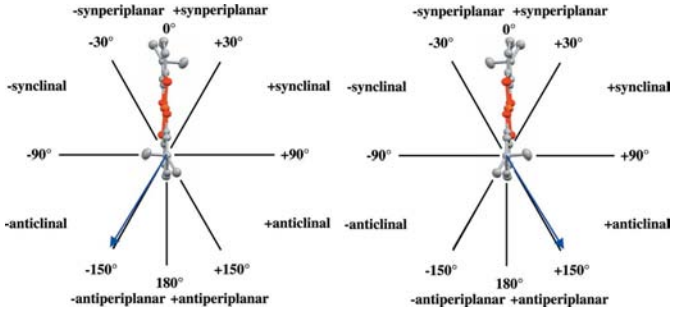


Figure 1
Projection diagrams of the isopropyl substituents in (IV), showing that the average methyl vector (arrow) for one of the isopropyl groups resides in the −anticlinal region of torsional space (left), while the other isopropyl group resides in the +anticlinal region (right). Hence, the use here of the designation (+*ac*,−*ac*), where the + and − signs indicate positive and negative torsion angle values.

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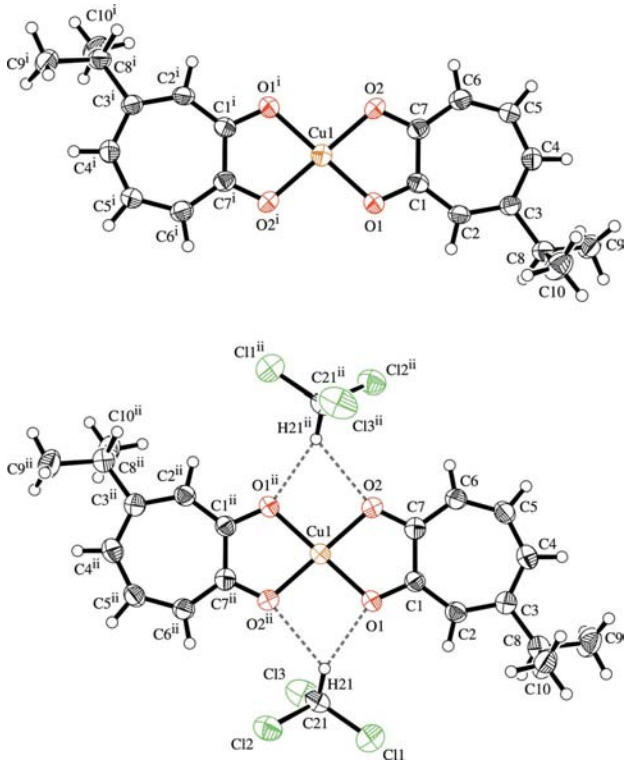

Figure 2
The molecular structures of (IV) (top) and (V) (bottom). Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. The second crystallographically independent chloroform disolvate, *i.e.* involving atoms Cu2, O3, O4, H22, C22, Cl4, Cl5 and C16, is statistically identical and therefore not shown. [Symmetry codes: (i) $2-x, 2-y, -z$; (ii) $1-x, 1-y, 2-z$.]

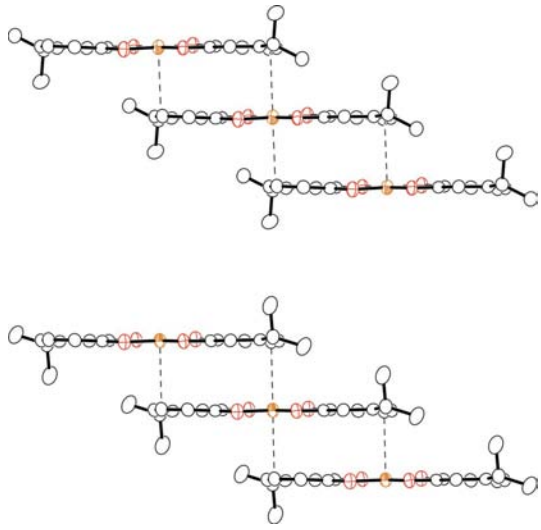

Figure 3
Stacking and π–π interactions in (IV) (top) and (V) (bottom). Displacement ellipsoids are drawn at the 50% probability level. The chloroform molecules in (V) have been omitted for clarity. The stacking involving the second independent disolvate is also equivalent and therefore not shown. All H atoms have been omitted.

Cu(hino)$_2$, has been established with certainty to be polymorphic.

Three polymorphs of *trans*-Cu(hino)$_2$ have been described previously in the literature, and we report here on a fourth polymorph and its chloroform disolvate. Polymorphs (I) (Barret *et al.*, 2002), (II) (Nomiya, Yoshizawa, Kasuga *et al.*, 2004; Arvanitis *et al.*, 2004) and (III) (Arvanitis *et al.*, 2004) contain (+*sp*,−*sp*)-*trans*-Cu(hino)$_2$, while the new polymorph, (IV), and its chloroform disolvate, (V), contain (+*ac*,−*ac*)-*trans*-Cu(hino)$_2$. The synperiplanar (*sp*) and anticlinal (*ac*) designators specify the average methyl orientation of each isopropyl group relative to the tropolone ring to which it is attached (see Fig. 1). The + and − signs with the *sp* designators are not standard nomenclature (Moss, 1996); they are used here to clarify that *sp* substituents can indeed possess positive and negative values, and to help specify whether the average methyl vectors are rotated slightly to one side or to opposite sides of the best plane through the molecule. Also, our convention is that a *syn*-isopropyl substituent will have its average methyl vector oriented inwards or towards the half of the tropolone molecule containing the metal atom, and conversely, an *anti*-isopropyl group will have its methyl vector directed outwards or away from the metal. Views of (IV) and (V) are given in Fig. 2, and comparative geometric parameters for (I)–(V) are summarized in Table 1.

Triclinic green–yellow plates of (IV) and grey–green plates of (V) were obtained by recrystallization of [*cis*-Cu(hino)$_2$]$_2$·[*trans*-Cu(hino)$_2$]$_2$·*trans*-Cu(hino)$_2$ from ethylene glycol–water and chloroform, respectively. The Cu centers in all forms of monomeric *trans*-Cu(hino)$_2$, *i.e.* (I)–(V), reside on centers of crystallographic inversion symmetry and have square-planar coordination geometries. The five atoms of the CuO$_4$ cores in these monomers are required by symmetry to be coplanar. All core bond distances and angles in (I)–(V), with the possible exception of (II), are statistically equivalent (see Table 1). Subtle structural variations do of course exist as one moves outwards away from the CuO$_4$ core. In (I) and (II), the Cu(tropolone)$_2$ moieties, *i.e.* excluding the isopropyl substituents, are best described as planar. In (III), a 7.1 (1)° folding along the O1···O2 vector is observed. In (IV) and (V), each half-moiety exhibits a 4.5 (2)° torsional twist (see Fig. 3). Clearly, any computational study regarding polymorph prediction for *trans*-Cu(hino)$_2$ would need to consider the conformational flexibility of the Cu(tropolone)$_2$ moiety, in addition to the rotational degrees of freedom of the isopropyl substituents and intermolecular packing interactions.

As shown in Table 1, the geometry at atom C3 is the most meaningful, and it should come as no surprise that the positioning and orientation of the isopropyl substituents should vary from one polymorph to another. In (I)–(III), the C2—C3—C8 angles are slightly smaller than the C4—C3—C8 angles, but all are near 117°. In (IV) and (V), C2—C3—C8 and C4—C3—C8 are significantly different, with the latter approaching 120°. The C2—C3—C8—*X* torsion angles in (I)–(III) are also noticably different from those in (IV) and (V). These are the hallmarks for (+*sp*,−*sp*) isopropyl substituents in (I)–(III) and for (+*ac*,−*ac*) isopropyl substituents in (IV) and (V). These angular and torsional differences are also observed in hinokitiol itself (Derry & Hamor, 1972; Ohishi *et*

al., 1994; Tanaka *et al.*, 2001), and are generally applicable to other metal hinokitiolate complexes as well (Nomiya *et al.*, 2009). Exceptions will inevitably occur with changes in coordination geometries.

The crystal structures of (II)–(V) are consistent with the presence of weak intermolecular Cu···olefin π interactions. With the exception of (I), the *trans*-Cu(hino)$_2$ molecules in these polymorphs pack into extended columns or stacks, such that the π-systems of neighboring molecules are positioned above and below each formally four-coordinate Cu center. Segments of that stacking for (IV) and (V) are shown in Fig. 3. The Cu center is 3.336 (1) Å from the centroid defined by atoms C1/C4–C7 in (II), and 3.226 (2), 3.290 (4) and 3.290 (4) Å from the centroid of the C4—C5 bond in (III)–(V), respectively. As in Table 1, the Cu···centroid distance and all other intermolecular contact distances given below for (V) correspond to averages over two independent molecules. For (IV) and (V), the closest contacts are actually shifted towards atom C5 and are 3.258 (4) and 3.214 (4) Å, respectively. These distances may be compared with values of 3.25–3.55 Å reported for longer-range noncovalent Cu···arene contacts (Mascal *et al.*, 2000). The distances between the least-squares planes through adjacent molecules, or stacking distances, are 3.336 (1), 3.235 (2), 3.311 (2) and 3.257 (2) Å for (II)–(V), respectively. The Cu···Cu distances between neighboring molecules within a stack are 5.1549 (3), 6.7470 (1), 6.3371 (2) and 6.1893 (2) Å for (II)–(V), respectively, and correspond to a unit translation in the crystallographic *a* direction for (II), (IV) and (V), and in the *b* direction for (III). The slippages (see Fig. 3) of one molecule from orthogonal coincidence with a neighboring molecule within a stack are 3.930 (1), 5.921 (2), 5.403 (2) and 5.263 (2) Å for (II)–(V), respectively. It is remarkable that, in spite of the presence of solvent molecules in (V), its *trans*-Cu(hino)$_2$ stacks are strikingly similar to those in (IV). The only visual difference in the segments shown in Fig. 3 would appear to be the orientations of the isopropyl groups. Clearly, the reader is encouraged to examine the numerical data above and not just illustrations when comparing such closely related structures.

Finally, each *trans*-monomer in (V) is also hydrogen bonded to two chloroform molecules, and so, not surprisingly, the chloroform molecules are also organized into columns running parallel to the crystallographic *a* axis. The bifurcated hydrogen bonding is shown in Fig. 2 and details are given in Table 2 [additionally, O1···H21···O2^{ii} = 74° for one of the crystallographically independent chloroform molecules in the asymmetric unit, and O3^{iii}···H22···O4 = 74° for the other; symmetry codes: (ii) $-x+1, -y+1, -z+2$; (iii) $-x+1, -y, -z+1$]. We are not aware of any published examples of bifurcated chloroform hydrogen bonds with metal tropolone complexes. However, there is a plethora of bifurcated chloroform hydrogen bonds with other complexes, among which are two examples containing square-planar CuO_4 cores (Maverick *et al.*, 1986; Pariya *et al.*, 2007). The distances and angles in those examples are C—H = 1.00 Å, H···O = 2.32–2.42 Å, C···O = 3.101–3.281 Å, C—H···O = 132–146° and O···H···O = 66–67°, similar enough to say that the hydrogen bonding in (V) is normal.

In summary, (+*ac*,−*ac*)-*trans*-Cu(hino)$_2$, (IV), and its chloroform disolvate, (V), have been crystallographically characterized. The hinokitiolate O atoms in (V) participate in hydrogen bonding. Hydrogen bonding was also previously observed in (III) (Arvanitis *et al.*, 2004). These observations are at odds with the suggestion that the formation of the CuO_4 core inhibits an interaction of the O atoms with microorganisms/proteins (Nomiya, Yoshizawa, Tsukagoshi *et al.*, 2004). If C—H···O(hino) hydrogen bonding is possible, surely the stronger N—H···O(hino) and O—H···O(hino) interactions are possible as well.

Experimental

[*cis*-Cu(hino)$_2$]$_2$·[*trans*-Cu(hino)$_2$]$_2$·*trans*-Cu(hino)$_2$ was prepared according to a literature procedure (Barret *et al.*, 2002). Room-temperature recrystallization by vapor diffusion of water into an ethylene glycol solution yielded green–yellow plates of (IV). Recrystallization from chloroform yielded grey–green plates of (V). The crystallographic quality of the latter degrades rapidly *via* solvent loss. Retaining a small amount of mother liquor, a blanket of chloroform vapor over the solids and/or speed in handling (V) are recommended.

Compound (IV)

Crystal data

$[Cu(C_{10}H_{11}O_2)_2]$
M_r = 389.92
Triclinic, $P\overline{1}$
a = 6.3371 (2) Å
b = 8.4915 (5) Å
c = 8.7216 (5) Å
α = 77.037 (2)°
β = 76.362 (3)°
γ = 80.093 (3)°
V = 440.93 (4) Å^3
Z = 1
Mo $K\alpha$ radiation
μ = 1.26 mm^{-1}
T = 200 K
0.20 × 0.10 × 0.02 mm

Data collection

Nonius KappaCCD area-detector diffractometer
Absorption correction: ψ scan (*SHELXTL*; Sheldrick, 2008)
T_{min} = 0.787, T_{max} = 0.975
8954 measured reflections
2006 independent reflections
1461 reflections with $I > 2\sigma(I)$
R_{int} = 0.084

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.065
$wR(F^2)$ = 0.204
S = 1.03
2006 reflections
118 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.53 e Å^{-3}
$\Delta\rho_{min}$ = −0.83 e Å^{-3}

Compound (V)

Crystal data

$[Cu(C_{10}H_{11}O_2)_2]\cdot 2CHCl_3$
M_r = 628.65
Triclinic, $P\overline{1}$
a = 6.1893 (2) Å
b = 8.4581 (3) Å
c = 25.7989 (10) Å
α = 95.730 (2)°
β = 91.884 (2)°
γ = 100.878 (3)°
V = 1317.82 (8) Å^3
Z = 2
Mo $K\alpha$ radiation
μ = 1.46 mm^{-1}
T = 200 K
0.23 × 0.13 × 0.03 mm

Table 1
Comparative geometric parameters (Å, °) for monomeric *trans*-Cu-$(C_{10}H_{11}O_2)_2$ polymorphs.

	(I)[a]	(II)[b]	(II)[c]
Cu1—O1	1.900 (2)	1.920 (2)	1.915 (2)
Cu1—O2	1.904 (3)	1.906 (2)	1.901 (2)
O1—C1	1.296 (5)	1.297 (4)	1.295 (3)
O2—C7	1.293 (5)	1.302 (4)	1.289 (4)
O1—Cu1—O2	83.84 (13)	84.06 (9)	83.70 (9)
Cu1—O1—C1	113.5 (3)	112.9 (2)	113.0 (2)
Cu1—O2—C7	113.5 (3)	113.4 (2)	113.5 (2)
C2—C3—C8	116.5 (4)	116.5 (3)	116.8 (3)
C4—C3—C8	117.4 (4)	116.8 (3)	117.4 (3)
C2—C3—C8—*X*	−4.6 (6)	12.4 (4)	−13.4 (4)
	(III)[c]	(IV)[d]	(V)[d]
Cu1—O1	1.918 (2)	1.915 (3)	1.908 (3)
Cu1—O2	1.913 (2)	1.911 (3)	1.904 (3)
O1—C1	1.292 (3)	1.301 (5)	1.300 (5)
O2—C7	1.293 (3)	1.297 (5)	1.304 (5)
O1—Cu1—O2	83.90 (8)	83.76 (12)	84.40 (12)
Cu1—O1—C1	112.9 (2)	112.9 (3)	112.9 (2)
Cu1—O2—C7	112.7 (2)	113.3 (3)	112.6 (3)
C2—C3—C8	116.5 (2)	115.5 (4)	114.8 (4)
C4—C3—C8	117.5 (3)	119.2 (4)	119.0 (4)
C2—C3—C8—*X*	0.9 (3)	−147.8 (6)	−142.8 (6)

References: (*a*) Barret *et al.* (2002); (*b*) Nomiya, Yoshizawa, Kasuga *et al.* (2004), corrected; (*c*) Arvanitis *et al.* (2004); (*d*) this work, where the values for (V) are averages over two independent molecules. Note: for each isopropyl substituent, *X* corresponds to the centroid of the two terminal methyl C atoms.

Table 2
Hydrogen-bond geometry (Å, °) for (V).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C21—H21···O1	1.00	2.26	3.167 (5)	151
C21—H21···O2^{ii}	1.00	2.43	3.138 (6)	127
C22—H22···O3^{iii}	1.00	2.31	3.214 (5)	149
C22—H22···O4	1.00	2.40	3.123 (5)	129

Symmetry codes: (ii) $-x+1, -y+1, -z+2$; (iii) $-x+1, -y, -z+1$.

Data collection

Nonius KappaCCD area-detector diffractometer
Absorption correction: ψ scan (*SHELXTL*; Sheldrick, 2008)
T_{min} = 0.734, T_{max} = 0.964
21329 measured reflections
4574 independent reflections
3392 reflections with $I > 2\sigma(I)$
R_{int} = 0.078

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.050
$wR(F^2)$ = 0.136
S = 1.04
4574 reflections
307 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.55 e Å^{-3}
$\Delta\rho_{min}$ = −0.62 e Å^{-3}

The structures of (IV) and (V) were determined from nonmerohedrally twinned data sets. The twin law for (IV) was [$\bar{1}$00/−0.338,1,−0.379/00$\bar{1}$] and corresponds to twinning by twofold rotation about the *a** axis. The contributions from the major and minor components of the twinning were 0.741 (6) and 0.259 (6), respectively. The twin law for (V) was [$\bar{1}$00/0$\bar{1}$0/0.447,0.671,1] and corresponds to twinning by twofold rotation about the *c** axis. The twinning was minor but still significant, with contributions of 0.961 (2) and 0.039 (2) from the major and minor components, respectively. The derivation of the twin laws and the subsequent generation of HKLF 5 data sets for refinements were achieved using *PLATON* (Spek, 2009).

All H atoms were allowed to ride on their respective C atoms, with C—H distances constrained to the *SHELXTL* (Sheldrick, 2008) default values for the specified functional groups at 200 K, *i.e.* 0.95, 1.00 and 0.98 Å for the tropolone, methine and methyl H atoms, respectively. The U_{iso}(H) values were set at 1.2U_{eq}(C) for the tropolone and methine H atoms, and 1.5U_{eq}(C) for the methyl H atoms.

For both compounds, data collection: *COLLECT* (Nonius, 1998); cell refinement: *DENZO-SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO-SMN*, *SHELXTL* (Sheldrick, 2008) and *PLATON* (Spek, 2009); program(s) used to solve structure: *SHELXTL*; program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL* and *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *SHELXTL*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FN3033). Services for accessing these data are described at the back of the journal.

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