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Probing systematic errors in experimental charge density by multipole and invariom modeling: a twinned crystal of 1,10-phenanthroline hydrate

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The modeling of experimental electron density in a twinned crystal of 1,10-phenanthroline hydrate within an invariom approach revealed its another advantage for charge density studies, which is assessing the reliability of chemically relevant information provided by a conventional multipole refinement against high-resolution X-ray diffraction data.

Electron density studies based on X-ray diffraction or quantum chemical calculations are very helpful in addressing important chemical problems in modern materials science and biology.[1] Despite ever-growing progress in this interdisciplinary field, there is still a room for further developments. Thus, an invariom approach[2] has recently emerged as a fast and versatile alternative to electron density analysis based on the multipole refinement of high-resolution X-ray diffraction data. Invarioms[2] are aspherical atomic scattering factors devised to replace spherical ones routinely employed in conventional crystal structure determination and calculated for an atom in a given covalent environment within the same multipole formalism widely used in conventional charge density studies. Although new, the invariom approach already proved to perform similarly well for systems accessible by the latter[4] and outperform them for systems that are not. Taking the multipole parameters computed at a high level of theory and stored in a database,[3] it offers the opportunities of retrieving an 'experimental' electron density distribution from low (normal) resolution datasets,[5–7] those collected with copper radiation[8] and/or for larger molecules with poor reflective power[9] and those suffering from a disorder.[10] This list of experimental pitfalls that do not allow achieving the level of accuracy required for the reliable determination of electron density features from X-ray diffraction data using conventional multipole refinement may be expanded by including another frequently encountered problem, the twinning.

To check if the invariom approach will be of any help in such a case, we performed a comparative study for commercially available 1,10-phenanthroline monohydrate[11] (Figure 1), an important building block in material chemistry.[12–15] Experimental electron density analysis for 1,10-phenanthroline monohydrate (hereinafter referred to as Phen)[†] seems a real challenge, as it gives crystals with three independent phenanthroline molecules and three water species in an asymmetric part of the unit cell, having modest reflective power and on top of that – being twinned by merohedry.

In agreement with previous X-ray diffraction data for Phen,[11] it has an infinite 3_2 (or 3_1) screw-chain H-bonded structure that we have solved in a space group $P3_2$, which is very prone to twinning. A detailed analysis of our data did reveal a partial

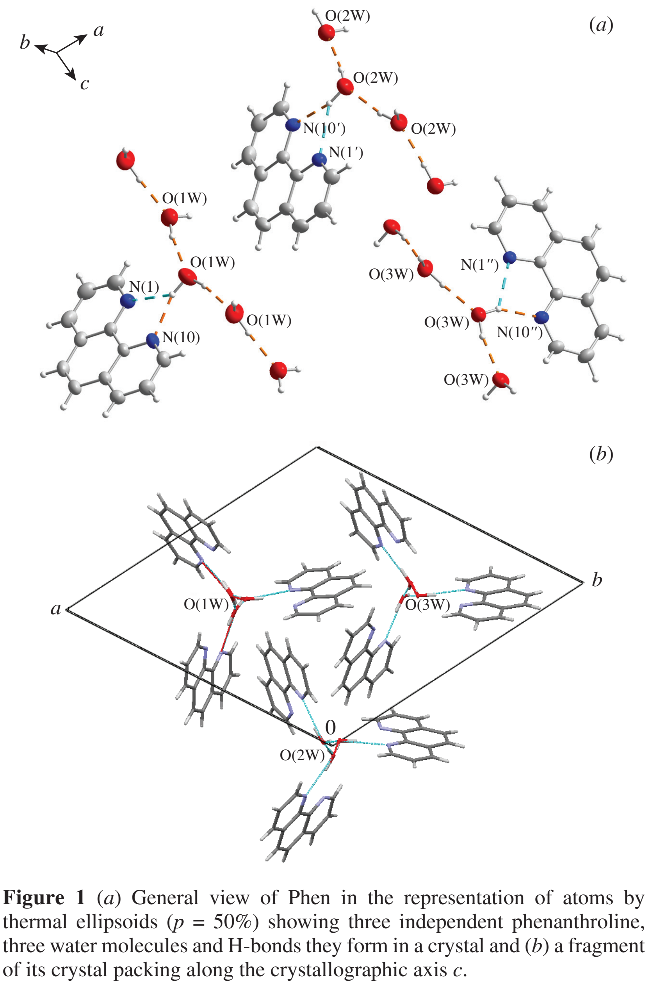

Figure 1 (*a*) General view of Phen in the representation of atoms by thermal ellipsoids (p = 50%) showing three independent phenanthroline, three water molecules and H-bonds they form in a crystal and (*b*) a fragment of its crystal packing along the crystallographic axis *c*.

twinning by a twofold rotation about the direction [2 1 0] corresponding to the crystallographic twofold symmetry axis of $P3_212$ (previously assumed to be the parent space group of Phen[11]); the fraction of the second individual is, however, so small (3%) that it was not even recognized at the beginning. Therefore, the collected dataset for Phen still might be suitable for a further electron density study through multipole refinement as having rather high resolution.

To determine how the presence of a partial twinning in Phen affects the electron density distribution in its crystal and whether the invariom approximation is able to provide any advantage

[†] CCDC 998980 and 998981 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2014.

over multipole refinement in dealing with it, we performed a comparative analysis between these two models with this twinning ignored and then taken into account and compared its results with those obtained from periodic quantum chemistry (see Online Supplementary Materials for experimental and computational details). Given that accessing weak interatomic interactions requires rigorous investigation of very fine features of electron density hardly available in this case, the main focus of our study is on covalent and hydrogen bonds, which were well described by an invariom approach[16–20] with the accuracy matching that of a full multipole refinement.[4]

A convenient approach towards quantifying the expected differences in chemical bonding parameters based on four resulting experimental electron densities (recovered by multipole or invariom modeling combined with or without an account for twinning) and a computed one (from periodic quantum chemical calculations) is the use of a topological analysis within the Bader's quantum theory of 'Atoms in Molecules' (QTAIM).[21] It provides a full set of bonding (stabilizing) interactions in a crystal, all identified by bond critical points (3, –1) (BCPs) and characterized by the values of electron density, its Laplacian, potential energy density, *etc*. Note that the latter is semi-qualitatively related to the energy of an interaction,[22,23] initially being an H-bond but then belonging to other types from H···H[24] to coordinate bonds;[25,26] this simple relation was repeatedly shown to provide highly accurate estimates.[27] An interaction energy thus evaluated provides a useful measure to compare a full set of hydrogen bonds formed by independent molecules of phenanthroline and water (they are three of each type in an asymmetric part of a unit cell; Figure 1) in Phen; these include bifurcated O–H···N and O–H···O bonds [O···N 2.9171(10)–2.9660(10)/3.1669(10)–3.2124(11) Å, ∠OHN 153.2(14)–156.5(15)/128.7(12)–132.6(13)° and O···O 2.9359(11)–2.9649(10) Å, ∠OHO 164(3)–167.9(19)°]. The latter assemble water molecules into three independent H-bonded chains along the crystallographic axis *c*; given that the above twin axis goes straight through these chains perpendicular to them, one may expect it to 'corrupt' electron density features of water molecules and hydrogen bonds they form in a crystal, as revealed from multipole or invariom refinement with and without an account for this twinning (see Online Supplementary Materials).

In both cases, multipole and invariom modeling of the experimental dataset resulted in deformation electron density (DED) distributions (Figure S1, Online Supplementary Materials) all being quite reasonable for phenanthroline molecules and featuring maxima along the covalent bonds and in the areas of electron lone pairs (LPs); these features improved significantly after an account for twinning or use of the invariom approximation. For water molecules, the distinction between the two models was even more pronounced. The multipole-derived DED distributions were not exactly as expected, lacking two distinct maxima corresponding to oxygen's LPs and O–H bonds and electron density depletions pointing towards LPs of nitrogen atoms. Those are clearly observed only in the case of the invariom model, which gave virtually identical DED maps whether the twinning was accounted for or not. The latter also mirror deformation electron density features obtained from periodic quantum chemical calculations of crystalline Phen.

In line with the improvement in DED distributions following the account for twinning and transfer to the invariom model, topological parameters of the intramolecular bonds (all found in search for BCPs) in Phen become more consistent between the independent species. The poorest agreement in electron density and its Laplacian in the corresponding BCPs is observed for the multipole refinement of the original dataset. In this case, the discrepancies are well above the 'transferability indices' (0.1 eÅ^{-3} and 3–4 eÅ^{-5}),[28] reaching as high as 0.36 eÅ^{-3} and 9.27 eÅ^{-5}. The account for twining (with 3% of the second component only) leads to a significant decrease in these values: in average, they become twice as small (0.16 eÅ^{-3} and 5.30 eÅ^{-5}) and approach the transferability indices. When derived from the invariom model, the two parameters are almost the same for all the independent molecules with the largest differences being less than 0.02 eÅ^{-3} and 0.55 eÅ^{-5}; the account for twinning causes their average values to vary by 0.01 eÅ^{-3} and 0.37 eÅ^{-5} only. Note that, if taken from periodic quantum chemical calculations for Phen with a geometry observed in the original X-ray diffraction dataset (see Online Supplementary Materials), electron density and its Laplacian in BCPs for all the covalent bonds in the phenanthroline species vary within 0.01 eÅ^{-3} and 0.43 eÅ^{-5}, falling in between those from invariom refinement against experimental data with and without twinning accounted for.

Deficiency of the electron density obtained by multipole modeling with no account for twinning emerges in intermolecular regions; however, only those that correspond to the hydrogen bonds will be inspected in more detail to make a reliable comparison between the four experimental and one theoretical models, as they should be described well by the invariom approximation.[7,8,17–19] Although all the hydrogen bonds for the crystalline Phen were identified as interactions of the closed-shell type [$\nabla^2\rho(\boldsymbol{r}) > 0$, $h_e(\boldsymbol{r}) > 0$] with low-to-medium strength according to their geometry, the topological parameters of multipole-derived experimental electron density with twinning ignored for some of them are very suspicious, having too high or too low values in comparison with others (Table S2, Online Supplementary Materials). Thus, the values of $\rho(\boldsymbol{r})$ in the BCPs belonging to the strongest component of the bifurcated O–H···N bonds are from 0.07 to 0.20 eÅ^{-3}, while those for the weaker component vary in a much narrower range of 0.04–0.06 eÅ^{-3}. Note that the largest difference in the interatomic O···N(10) and O···N(1) distances [2.9171(10)–2.9660(10) and 3.1669(10)–3.2124(11) Å] is the same in both cases [0.048(1) Å]. Disagreement is even more striking for the hydrogen bonds between the water molecules: variation in the distance O···O by 0.029(1) Å corresponds to the $\rho(\boldsymbol{r})$ values becoming nearly ten times higher (from 0.02 to 0.18 eÅ^{-3}).

As comparing numerous parameters for all the hydrogen bonds formed by several independent molecules and revealed from five model electron densities is not very convenient, an interaction energy will be used instead (Table 1), which is easily estimated through the Espinosa correlation[22,23] relating it to the potential energy density function $v(\boldsymbol{r})$ in a BCP. The interaction energies thus obtained clearly show that the multipole refinement of the original X-ray diffraction dataset not corrected for the partial twinning gives totally unreasonable results for the shortest O–H···N(10) and the longest O–H···O bonds having the energies of 8.1 (*vs*. 1.3–1.7 and 2.8–4.1) and 1.1 (*vs*. 6.3–7.4) kcal mol^{-1}, respectively. Going to the multipole model with this twinning taken into account causes the energy of these H-bonds to 'make more sense' (up to 3.5 kcal mol^{-1}), given that now all the values fall into the narrower ranges of 1.3–1.5, 3.5–4.0 and 3.5–6.1 kcal mol^{-1}. Those agree well with the modest variation in the corresponding donor–acceptor distances and satisfactory with the interaction energies estimated from periodic quantum chemistry (Table 1). In addition, the weaker O–H···N(1) bonds involving three independent phenanthroline molecules now become stronger with a decrease in the O···N distance, as it is expected but not observed in the case of the original dataset.

Note that despite significant improvements, the energy of the shortest O–H···O bond [O···O 2.9359(11) Å] still seems a bit higher, although it decreased from 7.4 to 6.1 kcal mol^{-1} upon accounting for twinning. Periodic quantum chemical calcula-

Table 1 Energy (in kcal mol^{-1}) of O–H···N and O–H···O bonds and net charges (in e)[a] of phenanthroline and water molecules in Phen based on the multipole and invariom (in parentheses) modeling of X-ray diffraction data with and without an account for twinning and those from periodic quantum-chemical calculations with original X-ray diffraction data used as a starting model.

Species	d/Å[b]	No account for twinning		With account for twinning		Quantum chemistry	
		$E_{\text{H-bond}}$	Charge	$E_{\text{H-bond}}$	Charge	$E_{\text{H-bond}}$	Charge
Phen1	**2.9179(13)**/3.2119(13)	**8.1 (5.4)**/1.7 (1.5)	**+0.29 (+0.01)**	**3.5 (5.4)**/1.3 (1.5)	**+0.09 (+0.01)**	**6.5**/1.5	–0.06
Phen2	2.9658(12)/3.1643(12)	2.8 (4.7)/1.3 (1.7)	–0.03 (–0.01)	4.0 (4.7)/1.5 (1.7)	–0.02 (–0.01)	5.4/1.9	–0.05
Phen3	2.9180(12)/3.1827(11)	4.1 (5.5)/1.5 (1.5)	–0.32 (–0.01)	4.0 (5.5)/1.4 (1.5)	–0.19 (–0.01)	6.3/1.8	–0.04
O(1W)	2.9359(11)	7.4 (4.7)	**+0.23 (0.00)**	6.1 (4.7)	**+0.17 (0.00)**	4.6	+0.06
O(2W)	**2.9649(10)**	**1.1 (4.5)**	–0.06 (+0.01)	**3.5 (4.4)**	+0.03 (+0.01)	**4.8**	+0.05
O(3W)	2.9374(9)	6.3 (4.7)	–0.08 (+0.01)	4.0 (4.7)	–0.09 (+0.01)	5.2	+0.04

[a] Obtained from the experimental electron densities, charge leakage varies from 0.003 e (multipole refinement with an account for twinning) to 0.02 e (multipole refinement with no account for twinning); invariom refinement gives a charge leakage of less than 0.01 e in both cases. The sum of atomic volumes (744.5–745.5 Å^3) reproduces well the volume of an independent part of the unit cell (747.4 Å^3) with a relative error less than 0.4%. Although integrated Lagrangian [$L(r) = -{}^1/_4\nabla^2\rho(\mathbf{r})$] for every atomic basin has to be exactly zero, a reasonably small value averaging to 0.4×10^{-3} a.u. was obtained; the largest one (4.5×10^{-3} a.u.) is observed for the oxygen atom of the water molecule H_2O(2W) from the multipole refinement of the original dataset and decreases to 0.6×10^{-3} a.u. after the account for twinning. [b] d stands for the distance between a donor and an acceptor of proton.

tions give a value of 5.2 kcal mol^{-1} as compared with 4.6 and 4.8 kcal mol^{-1} for the other two O–H···O bonds in the crystal of Phen. For comparison, the energy of 5.2–9.0 kcal mol^{-1} was likewise assigned to hydrogen bonds with O···O distances between water molecules being 2.6764(7)–2.8674(6) Å in an earlier reported tetrahydrate of piperidine-2-carboxylic acid.[29]

At the same time, the electron densities obtained by the invariom modeling have none of these 'artifacts' of twinning suffered by the crystalline Phen. Whether the original dataset or the corrected one is used, it gives the energies of hydrogen bonds that are more consistent with each other (Figure S2) and with those for the above tetrahydrate.[29] Within each group (the two components of the bifurcated O–H···N and O–H···O bonds), the corresponding values estimated through the Espinosa correlation vary within 1.5–1.7, 4.7–5.5 and 4.4–4.7 kcal mol^{-1} only. Both on the absolute and relative scales, the latter show the best agreement with the quantum chemical estimates for these hydrogen bonds (1.5–1.9, 5.4–6.5 and 4.6–5.2 kcal mol^{-1}); the multipole refinement of the dataset accounted for the twinning being second to it (1.3–1.5, 3.5–4.0 and 3.5–6.1 kcal mol^{-1}) and that of the original dataset providing the worst results (1.3–1.7, 2.8–8.1 and 1.1–7.4 kcal mol^{-1}).

The deficiency of a conventional multipole refinement in our case is, apparently, a result of atomic positions, atomic displacement parameters and multipole populations being refined against a twinning-affected dataset, although it significantly improved after an account for twinning. In the invariom model, only the first two parameters (together with a scaling factor) are refined against an experimental dataset[2] while others are taken from the invariom database;[3] thus, the resulting electron density is less sensitive to 'issues' with X-ray diffraction data and therefore provides a more reliable (and consistent) description of interatomic interactions in a crystal. In this case, the minor difference in the energy of hydrogen bonds between the two invariom models (below 0.1 kcal mol^{-1}) results from minor variations in their geometrical parameters upon accounting for twinning (Table S2).

The performance of the multipole and invariom refinements in quantifying the hydrogen bonds in Phen with and without the account for twinning mirrors that in describing charge distribution between the independent molecules in its crystal. Those are very different when taken from the multipole refinement against the original dataset, quite different when the twinning is accounted for and nearly the same when the invariom model is used (Table 1). While the latter gives identical charges for chemically identical species by definition, small variations in the parameters of hydrogen bonds and weak interactions, which are beyond the scope of this study [as they should be probe with care even in an ideal case (no twinning, disorder or weak reflective power)], may be expected to make net charges of symmetry-independent molecular species in Phen non-equivalent.[30] Indeed, those obtained by periodic quantum chemistry do not deviate much from the neutrality and vary within 0.02 e only, being the closest to the net charges estimated from the invariom-derived electron densities.

In contrast, the multipole refinement with no account for twinning gave a too high absolute value for the water molecule (+0.23 e) and the phenanthroline molecule (+0.29 e) that are involved in the O(1W)–H···N bond with an unreliable energy of 8.1 kcal mol^{-1}. In this case, one of the other phenanthroline species also has a charge that is very different from neutrality (–0.32 e). All these parameters decrease (by the absolute value) considerably with the account for twinning; a still suspicious net charge for H_2O(1W) (+0.17 e) agrees with its O–H···O bond being slightly stronger (6.1 kcal mol^{-1}) than expected.

Therefore, the features of electron density distribution as revealed by the multipole refinement of a corrupted dataset should be considered with care, since the account for such a small twinning as observed in Phen (3%) causes their dramatic changes; the invariom refinement does not suffer from that at all. This reveals a new advantage of invariom application for charge density studies, which is providing reliable and robust information on chemical bonding in terms of both interaction energies and net charges for twinned samples.

Thus, the list of experimental pitfalls that it allows dealing with from X-ray diffraction data now includes, among other frequently encountered problems such as weak reflective power[5–9] and disorder,[10] the twinning. Since those are not always recognized if their contribution is as low as in Phen, the invariom model may be used (in addition to the Hirshfeld test[31] or transferability indices[28]) to judge the quality of the electron density obtained by a conventional multipole refinement and not only *vice versa*, as was the case so far.

Periodic quantum chemical calculations also suitable for the same purpose are too time- and resource-consuming, while the invariom refinement takes seconds and does equally well for routine X-ray diffraction datasets; those can be quickly acquired on the spot, obtained elsewhere or even replaced by other data on starting geometries, *e.g.*, from NMR spectroscopic data.[4]

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2014.09.013.

References

1 C. Gatti and C. F. Matta, *Modern Charge-Density Analysis*, Springer, Berlin, 2012.
2 B. Dittrich, T. S. Koritsansky and P. Luger, *Angew. Chem. Int. Ed.*, 2004, **43**, 2718.
3 B. Dittrich, C. B. Hubschle, K. Propper, F. Dietrich, T. Stolper and J. J. Holstein, *Acta Crystallogr., Sect. B*, 2013, **69**, 91.
4 J. J. Holstein, C. B. Hubschle and B. Dittrich, *CrystEngComm*, 2012, **14**, 2520.
5 B. Dittrich, C. B. Hubschle, J. J. Holstein and F. P. A. Fabbiani, *J. Appl. Crystallogr.*, 2009, **42**, 1110.
6 C. J. Schurmann, K. Propper, T. Wagner and B. Dittrich, *Acta Crystallogr., Sect. B*, 2012, **68**, 313.
7 P. Luger, M. Weber, C. Hubschle and R. Tacke, *Org. Biomol. Chem.*, 2013, **11**, 2348.
8 B. Dittrich, M. Weber, R. Kalinowski, S. Grabowski, C. B. Hubschle and P. Luger, *Acta Crystallogr., Sect. B*, 2009, **65**, 749.
9 B. Dittrich, T. Koritsanszky, A. Volkov, S. Mebs and P. Luger, *Angew. Chem. Int. Ed.*, 2007, **46**, 2935.
10 J. J. Holstein, P. Luger, R. Kalinowski, S. Mebs, C. Paulmann and B. Dittrich, *Acta Crystallogr., Sect. B*, 2010, **66**, 568.
11 Y.-P. Tian, C.-Y. Duan, X.-X. Xu and X.-Z. You, *Acta Crystallogr., Sect. C*, 1995, **51**, 2309.
12 P. G. Sammes and G. Yahioglu, *Chem. Soc. Rev.*, 1994, **23**, 327.
13 K. Binnemans, P. Lenaerts, K. Driesena and C. Görller-Walranda, *J. Mater. Chem.*, 2004, **14**, 191.
14 L.-L. Li, K.-J. Lin, C.-J. Ho, C.-P. Sunb and H.-D. Yang, *Chem. Commun.*, 2006, 1286.
15 G. Accorsi, A. Listorti, K. Yoosaf and N. Armaroli, *Chem. Soc. Rev.*, 2009, **38**, 1690.
16 B. Dittrich and M. A. Spackman, *Acta Crystallogr., Sect. A*, 2007, **63**, 426.
17 R. Kalinowski, B. Dittrich, C. B. Hubschle, C. Paulmann and P. Luger, *Acta Crystallogr., Sect. B*, 2007, **63**, 753.
18 M. Weber, S. Grabowski, A. Hazra, S. Naskar, S. Banerjee, N. B. Mondal and P. Luger, *Chem. Asia J.*, 2011, **6**, 1390.
19 J. Bacsa, M. Okello, P. Singh and V. Nair, *Acta Crystallogr., Sect. C*, 2013, **69**, 285.
20 N. Dadda, A. Nassour, B. Guillot, N. Benali-Cherif and C. Jelsch, *Acta Crystallogr., Sect. A*, 2012, **68**, 452.
21 R. F. W. Bader, *Atoms in Molecules. A Quantum Theory*, Clarendon Press, Oxford, 1990.
22 E. Espinosa, E. Molins and C. Lecomte, *Chem. Phys. Lett.*, 1998, **285**, 170.
23 E. Espinosa, I. Alkorta, I. Rozas, J. Elguero and E. Molins, *Chem. Phys. Lett.*, 2001, **336**, 457.
24 K. A. Lyssenko, A. A. Korlyukov and M. Yu. Antipin, *Mendeleev Commun.*, 2005, 90.
25 A. O. Borissova, A. A. Korlyukov, M. Y. Antipin and K. A. Lyssenko, *J. Phys. Chem. A*, 2008, **112**, 11519.
26 L. N. Puntus, K. A. Lyssenko, M. Y. Antipin and J.-C. G. Bunzli, *Inorg. Chem.*, 2008, **47**, 11095.
27 K. A. Lyssenko, *Mendeleev Commun.*, 2012, **22**, 1.
28 L. Checinska, S. Mebs, C. B. Hubschle, D. Forster, W. Morgenroth and P. Luger, *Org. Biomol. Chem.*, 2006, **4**, 3242.
29 K. A. Lyssenko, Yu. V. Nelyubina, R. G. Kostyanovsky and M. Yu. Antipin, *ChemPhysChem*, 2006, **7**, 2453.
30 Yu. V. Nelyubina, M. Yu. Antipin, I. A. Cherepanov and K. A. Lyssenko, *CrystEngComm*, 2010, **12**, 77.
31 F. L. Hirshfeld, *Acta Crystallogr., Sect. A*, 1976, **32**, 239.

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