Incorrect tautomer assignment in crystal structures of 1,2,4-triazoles

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We proudly assert that a small-molecule crystal structure definitively locates all atoms. Coordinates are expected for all hydrogen atoms, and modern software conveniently places them in calculated positions after cursory inspection of a difference electron density map or none at all. However, 1,2,4-triazole structures should give us pause. The electron density of unprotonated N: looks fairly similar to N-H and C-H groups. High-level \textit{ab initio} calculations (Balabin, 2009) show the 1H tautomer of 1,2,4-triazole to be more stable than the 4H by 6.25 kcal mol\(^{-1}\).

\[ \text{H} \begin{array}{c} \text{N} \\ \text{N} \end{array} \text{N} \quad \text{OR} \quad \text{H} \begin{array}{c} \text{N} \\ \text{N} \end{array} \text{NH} \]

Unsurprisingly, a search of the November 2018 edition of the Cambridge Structural Database for neutral 1,2,4-triazoles yielded 203 hits in the 1H form and only 7 hits in 4H. But are even these 7 legitimate? CLTRZL and JUGYOB were subsequently redetermined (CLTRZL01, JUGYOB01) as 1H; comparing their geometric parameters helpfully shows which are indicative of the tautomeric form. Because N1-H…N4 hydrogen bonds (HB) link both into chains, the electron density gives little clue to which N atom is protonated. Even worse, the differences in distance between the formally single N1-C5 and formally double N2-C3 bonds of <=0.022 Å misleadingly suggest that N1 and N2 may be identical and N4 is different. Only the endocyclic bond angles, affected by valence shell electron pair repulsion, are unambiguous: the angle at protonated N1 exceeds that at N2 or N4 by 6° or more. For the remaining 5 structures CheckCIF is silent about the tautomeric form except where an N-H group without acceptor or a clash is found. DAMTRZ21 should be 1H since it has similar cell dimensions to 3 earlier 1H structures and its angle at N1 exceeds the others by =>5°. With its largest angle at N1 and a clash of “bare” N atoms MAJSOH should be changed to the 1H tautomer. The endocyclic angles in FALDAZ with its two independent triazole moieties suggest that both should be 1H, creating more HB. Surprisingly, FUZPOH is devoid of actual or possible N-H…N HB, but changing tautomer to 1H facilitates C-H…N HB. DEGNIM is credible as a 4H tautomer: although the angles are ambiguous, the triazole ring is incorporated in a crown ether enveloping a water molecule which can accept a HB from N4-H and stabilise it. Neutron diffraction would be very helpful to resolve ambiguities.