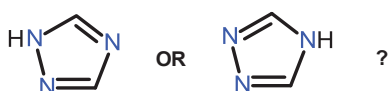


Incorrect tautomer assignment in crystal structures of 1,2,4-triazoles

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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 *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.



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 $\approx 5^\circ$. 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.

Balabin, R. M. (2009) J. Chem. Phys., 131, 154307_1-8.