Structure of Acetaminophen alias Paracetemol or Tylenol at the Atomic Level

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Abstract. The recent new rapid technique of determining structures of molecules by CryoEM Method microED techniques by Gonen et al, aroused the interest to compare the reported bond lengths for acetaminophen with the additivity of adajacent atomic radii rule. The latter was found by the author to explain the bond lengths in many small as well as large molecules. The bond distances obtained by conventional methods and those found by Grunen et al by electron diffraction agree well with the additivity rule, whereas those by the Gonen group seem slightly smaller. A possible reason is discussed here.

Introduction

Acetaminophen, also known [1] as tylenol or paracetemol is used as a mild pain and fever reducer (provided it is not overdosed!). It has the skeletal structure shown in Fig. 1:

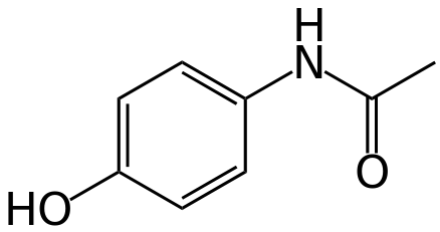


Fig. 1. Skeletal formula of acetaminophen, $C_8H_9NO_2$ from [1].

This was one of the many small molecules recently studied [2] by a new and rapid technique, 'The CryoEM Method MicroED'[3] and by electron diffraction [4]. The Fig below is from [3]:

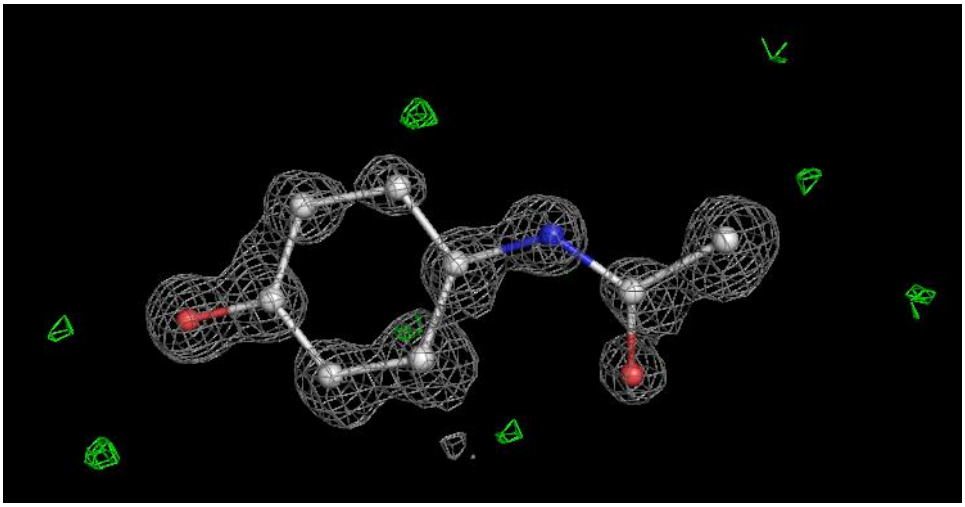
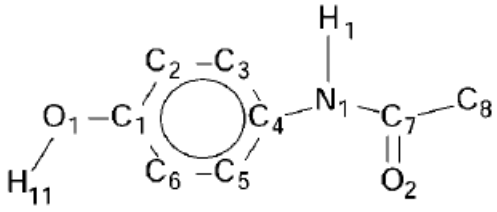


Fig. 2. Structure of acetaminophen, from [3].

This above structure tempted the author to try how far it conforms with the known bond lengths [5,6] and the additivity of radii rule found for many small as well as large molecules [7].

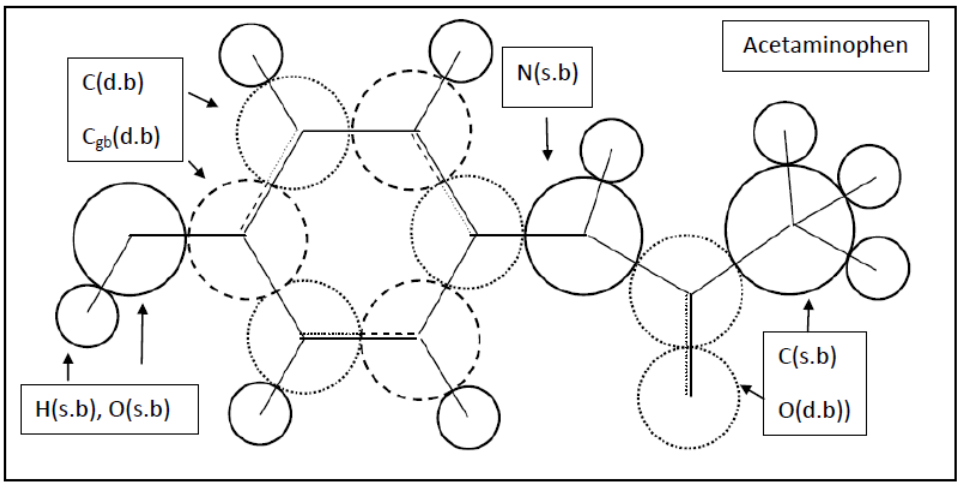
Results

The available bond length data from CCDC for the references {3-7] are collected in Table 1. The bond numbering in Table 1 is as per the notation in [6]. Atomic radii data for the various atoms in Fig. 3 were taken from [7] to obtain the radii sums as bond lengths tabulated in Table 1. The resulting structure (drawn to scale) is shown in Fig. 4.



Paracetamol, with atomic numbering scheme.

Fig. 3. Paracetemol structural formula from [5].



Atoms:	H(s.b),	O(s.b),	C_{gb}(d.b),	C(d.b),	N(s.b),	O(d.b),	C(s.b)
Radii (in A):	0.37,	0.67,	0.71,	0.67,	0.70,	0.60,	0.77

Fig. 4. Structure at the atomic level of acetaminophen (drawn to scale) with bond lengths as sums of the radii of adjacent atoms. The subscripts s.b, d.b and g.b, stand for single bond, double bond and graphite/graphene bond. The values of radii from [7] are given underneath the Figure.

Table 1. Comparison of bond lengths in acetaminophen

	series 1	series 2	series 3	series 4	series 5
Ref.	**[7]**	**[6]**	**[5]**	**[3]**	**[4]**
$H_{11}O_1$	**1.04**	**0.90**	**0.89**		**1.00**
O_1C_1	**1.38**	**1.37**	**1.38**	**1.21**	**1.40**
C_1C_2	**1.38**	**1.39**	**1.39**	**1.29**	**1.37**
C_2C_3	**1.38**	**1.38**	**1.39**	**1.27**	**1.33**
C_3C_4	**1.38**	**1.39**	**1.39**	**1.30**	**1.40**
C_4C_5	**1.38**	**1.40**	**1.39**	**1.27**	**1.30**
C_5C_6	**1.38**	**1.39**	**1.39**	**1.34**	**1.48**
C_6C_1	**1.38**	**1.39**	**1.39**	**1.30**	**1.32**
C_4N_1	**1.37**	**1.42**	**1.43**	**1.36**	**1.46**
N_1C_7	**1.37**	**1.34**	**1.34**	**1.24**	**1.32**
C_7O_2	**1.27**	**1.24**	**1.23**	**1.11**	**1.27**
C_7C_8	**1.44**	**1.51**	**1.51**	**1.43**	**1.42**
C_2H	**1.04**	**0.97**	**0.95**		**1.10**
C_3H	**1.08**	**0.97**	**0.96**		**1.10**
C_5H	**1.08**	**0.94**	**0.93**		**1.10**
C_6H	**1.04**	**0.98**	**0.98**		**1.10**
C_8H, av	**1.14**	**0.96**	**0.97**		**1.08**
N_1H_1	**1.07**	**0.93**	**0.90**		**1.03**

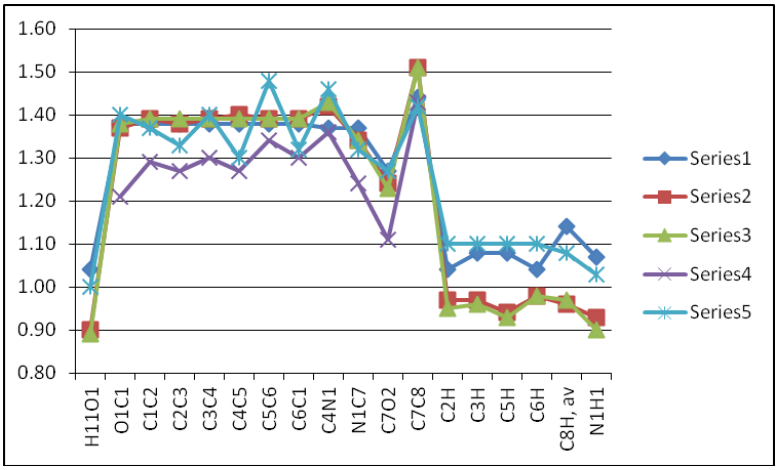


Fig. 5. Comparison of bond lengths in acetaminophen from various sources

Discussion

Fig. 5 shows a comparison of the bond length data in Table 1. It can be seen from the Figure and the data that the conventional methods [5,6] and the electron diffraction data [4] agree with the bond lengths obtained by the author as sums of radii of adjacent atoms. This confirms the additivity rule of radii in bond lengths. The values in [4] seem to be slightly smaller. The C_2C_3 and C_4C_5 bonds of lengths 1.27 A are lower than the benzene bond length of 1.38 A. This makes the average CC bond distance in benzene equal to 1.3 A. It might indicate that the structure perhaps shrinks at the conditions of the experiment, and the CC bond distance is approaching that of a triple bond [8].

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