Anti-malarial agent design using Pharmacoinformatics

Prasad V. Bharatam
Department of Medicinal Chemistry
National Institute of Pharmaceutical Education and Research (NIPER)
pvbharatam@niper.ac.in

Divalent N(I) compounds (**::**N(←L)$_2$⊕) are systems with bicoordinated nitrogen in N(I) formal oxidation state. This class of compounds contained all the pharmacophoric features developed through molecular modeling analysis. In protonated form guanylthiourea derivatives show divalent N(I) character which is essential to predict the activity of the active moiety. Anti-malarial agents proguanil, pyrimethamine and cycloguanil carry this property. This class is further being developed as a potential nucleus for antimalarial drug therapy. *In vitro* studies were carried out and two compounds from this class have shown activity in micro-molar range (100µM and 400nM).

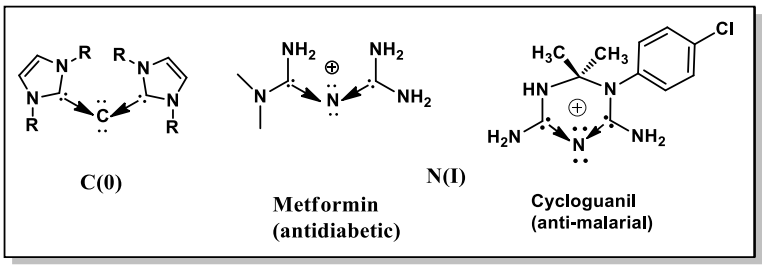

Fig. Structural representation of C(0) and N(I) species

References

1. D. Kathuria …P.V. Bharatam	**Org. Biomol. Chem.**	2019	17	8486-8521
2. D.P. Kale, ….P.V. Bharatam	**Mol. Pharmaceutics**	2019	16	2980-2991
3. N. Patel, R. Sood, P.V. Bharatam	**Chem. Rev.**	2018	118	8770-8785
4. N. Patel, … P.V. Bharatam	**Chem. Eur. J.**	2018	24	6418-6425.
5. …N. Tripathi….P.V. Bharatam	**Oncotarget**	2017	8	248-267
6. … PV Bharatam, A.K. Chakraborti	**J. Org. Chem.**	2017	82	10077-10091
7. P.V. Bharatam, …M. Arfeen	**Chem. Eur J.**	2016	22	1088-1096
8. ..P.V Bharatam… S. Bharate	**Chem. Commun.**	2016		1009-1012
9. G.K. Rastogi, … Bharatam, Tandon	**ACS Med. Chem. Letts.**	2015	6	1065-1070
10. A. Kusunuru, … Bharatam,	**Org. Letts.**	2015	17	3742-3745
11. A. Bhaviskar, … P.V. Bharatam	**ACS Med. Chem. Lett.**	2015	6	481-485
12. ... P.V. Bharatam ... S. Bharate	**Chem. Commun.**	2014		12076-12079
13. A. Baviskar, … P.V. Bharatam…	**J. Med. Chem.**	2011	54	5013-5030
14. D.S. Patel …… P.V. Bharatam	**J. Org. Chem.**	2011	76	2558-2567
15. L.S. Moon, ….PV. Bharatam	**J. Org. Chem.**	2010	75	5487-5498
16. D.S. Patel, . …P.V. Bharatam	**Chem. Commun.**	2009		1064-1066
17. S.V. Kessar,…. P.V. Bharatam, ...	**Angew. Chem. Int. Ed.**	2008	47	4703-4706
18. S.V. Kessar, ...P.V. Bharatam	**J. Am. Chem. Soc.**	2007	129	4506-4507
19. P. V. Bharatam, D.S. Patel, P. Iqbal.	**J. Med. Chem.**	2005	48	7615-7622.
20. S. Khanna, …. P. V. Bharatam	**J. Med. Chem.**	2005	48	3015-3025