

Advances in Understanding of Chemical Bonding: Inputs from Experimental and Theoretical Charge Density Analysis

Deepak Chopra*

Department of Chemistry, Indian Institute of Science Education and Research, Bhopal 462023, India

ABSTRACT: The development of charge density analysis has undergone a major renaissance in the last two decades. In recent years, the characterization of bonding features associated with atoms in molecules and in crystals has been explored using high-resolution X-ray diffraction data (laboratory or synchrotron) complemented by high level ab initio theoretical calculations. The extraction of one electron topological properties, namely, electrostatic charges, dipole moment and higher moments, electrostatic potential, electric field gradients, in addition to evaluation of the local kinetic and potential energy densities, have contributed toward an understanding of the electron density distributions in molecular solids. New topological descriptors, namely, the source function (SF) and electron localization function (ELF) provide additional information as regards characterization of the topology of the electron density. In addition, delocalization indices have also been developed to account for bonding features pertinent to M–M bonds. The evaluation of these properties have contributed significantly toward the understanding of intra- and intermolecular bonding features in organic, inorganic, and biomolecules in the crystalline phase, with concomitant applications in the understanding of chemical reactivity and material/biological properties. In recent years, the focus has strongly shifted toward the understanding of structure–property relationships in organometallic complexes containing labile M–C bonds in the crystal structure with subsequent implications in catalysis. This perspective aims to highlight the major developments in electron density measurements in the past few years and provides pointers directed toward the potential use of this technique in future applications for an improved understanding of chemical bonding in systems that have been unexplored.

$$\rho(\mathbf{x}, \mathbf{y}, \mathbf{z}) = 1/V \int \int \int F(\mathbf{hkl}) \exp[-2\pi i(\mathbf{hx} + \mathbf{ky} + \mathbf{lz})]$$

Reciprocal space

Charge Density [$\rho(\mathbf{x}, \mathbf{y}, \mathbf{z})$] defines the chemistry of the compound.

1. INTRODUCTION

The importance of X-ray diffraction (both powder and single crystal) has already been realized in the determination of the atomic positions in crystals and evaluation of the geometrical structure of crystals and molecules.¹ In the past few decades, the focus has shifted toward an understanding of the bonding features between atoms in molecules, the role of electron density in defining the chemistry in the molecule. A topological analysis of this quantity allows for an evaluation of the relationship between the nature of bonding and the chemical reactivity of the molecule. The quantification of electron density and the associated energetics in both intra- and intermolecular space in molecules in crystalline solids is thus of extreme interest.

A number of authoritative reviews² in the subject bring out the significance of charge density analysis aimed toward an understanding of chemical bonding in different molecular systems. Some of the important textbooks published in this area highlight the experimental³ and theoretical aspects⁴ related to the study of atoms in molecules (AIM) approach. The reader is advised to refer to an excellent textbook by Tsirelson and Ozerov to appreciate the theoretical foundations that form the basis of charge density research.⁵ A book by G. A. Jeffrey and J. F. Piniella reflects the applications of such analysis applied to chemical and biological systems with implications in drug

design.⁶ The latest developments in the area of charge density have been recently incorporated in a new textbook entitled “Modern Charge Density Analysis”,⁷ edited by C. Gatti and P. Macchi. In this perspective, it is of interest to bring to the notice of the scientific community the recent developments in the field of charge density research and the derived output that enables a comprehensive understanding of chemical bonding in organic, inorganic, metal–organic compounds, macromolecules, and organometallic systems.

2. EXPERIMENTAL PREREQUISITES FOR MEASUREMENT OF ACCURATE ELECTRON DENSITIES

The field of charge density research has achieved tremendous success primarily because of the increased advancements made in the field of technology. In addition to the default requirement of high-quality crystals, the development of instrumentation as regards the availability of charge-coupled device (CCD) detectors (ensures measurement of a significant number of reflections from a given region of reciprocal space),

Received: June 22, 2012

Revised: August 22, 2012

Published: August 28, 2012



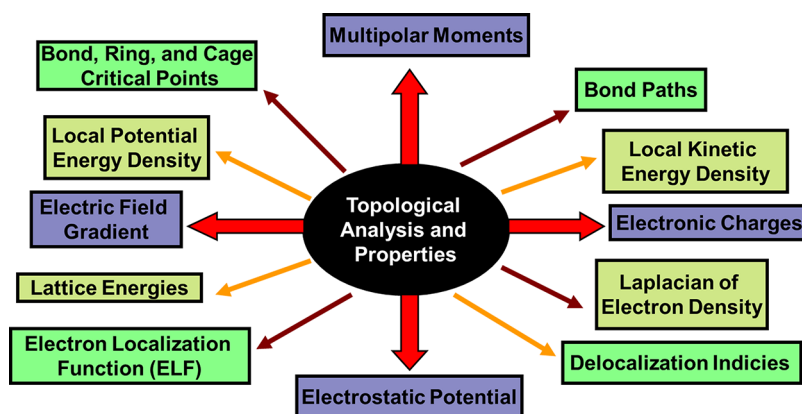


Figure 1. Chart representing the different properties derived from a topological analysis of the electron density distribution in solids (both experimental and theoretical).

low temperatures (nitrogen and helium cryogenics) to reduce thermal diffuse scattering and anharmonicity, high intense monochromatic wavelengths (use of rotating anode for the purpose of maximum extent of diffraction, i.e., high values of $\sin\theta/\lambda$ in diffraction space), and synchrotron radiation (variable wavelengths, in cases where the weak reflections are to be measured accurately and artifacts related to absorption and extinction eliminated)⁸ have contributed immensely toward the advancement made in the area of experimental electron density measurements. In addition, the integration programs related to data reduction procedures have also undergone significant development. Because of all the above-mentioned advantages, it is now possible to collect high quality accurate charge density data with high-resolution at low temperature in a day.⁹ The data collection protocols at the synchrotron source have been extensively developed for application in small molecules and also macromolecules.¹⁰ A detailed article highlighting the role of radiation sources, cryogenics, area detectors [2-D], validation of experimental data collected from different sources, importance of statistical plots, data reduction strategies with implications in multipole refinements, and the derived topological parameters brings out the important fact that electron density analysis is extremely sensitive and related to optimization of different related experimental factors.¹¹

3. MODELING THE ELECTRON DENSITY: THEORY AND DERIVATION OF TOPOLOGICAL PROPERTIES

The measurement of accurate charge density data and the subsequent analysis of the topological parameters can be obtained from a high-resolution X-ray diffraction experiment performed at low temperatures. The experimental electron density is then modeled using the Hansen–Coppens multipole formalism.^{12a} The program XD^{12b} is widely used for the topological analysis of charge densities. The modeling of the charge density features of an atom essentially consists of contribution from the core, the valence shell (quantification using the expansion and contraction term (κ) parameter), and the deformation of the valence shell, modeled using normalized spherical harmonics and the radial contribution functions (quantification using expansion and contraction (κ^1) parameter). The total electron density in the crystal is (both time and space averaged) then a summation of atom-centered charge distribution. The derived electron density is then subjected to Bader’s quantum theory of atoms in molecules.¹³ The position of the atom corresponds to local maxima at the nuclei. The

existence of a bond between two atoms is expressed by a set of topological parameters; the analysis is based on the identification of critical points, this being classified by the Hessian matrix of the electron density. In addition to bond critical points (defined as the position wherein the gradient of the electron density is zero), the bond path¹⁴ between two atoms defines the position of maximum electron density along the interaction length R_{ij} (not the interatomic vector). The second derivative of the electron density is referred to as the Laplacian, the magnitude and sign of this is indicative of the nature of chemical bonding between two atoms. A negative value represents shared interaction and a positive value represents closed shell interaction. The basics of electron density investigations are neatly summarized in a tutorial review.¹⁵ In recent years, additional topological parameters [Figure 1], namely, the electron localization function (ELF) introduced by Becke and Edgecombe¹⁶ and the Source function introduced by Bader and Gatti,¹⁷ have proven to be useful. In addition, electron delocalization indices $\delta(A,B)$ of Bader and Stephens¹⁸ (number of electron pairs delocalized between atoms A and B) have been derived to account for more sensitive aspects like conjugation and ionicity and hence to probe related aspects of chemical reactivity in molecules. Furthermore, an estimate of such topological parameters for an understanding of intra- and intermolecular interactions (namely, electrostatic forces and short and long H-bonds) in crystalline solids is also of relevance. These interactions are all pervasive in nature and exist in complex chemical and biological systems as well.¹⁹ Before any accurate estimates can be made about the topological estimates of H-bonds, it is of interest to realize the advancements made in the treatment of H-atoms during multipole refinements, these being extremely sensitive to the position and the thermal motion of these atoms. It has been observed that the static electron density is biased due to the incorrect position of the H-atoms and uncorrected deconvolution of the related thermal motion. The former problem was overcome by the use of neutron diffraction data, although the availability of large sized crystals places an important constraint on such studies. The latter is more complex, and an isotropic refinement of H-atom motion is far from satisfactory. Hence, it was realized that H-atoms, like the non-H atoms, also vibrate anisotropically and hence consist of a combination of both rigid body motion (due to anisotropic displacement parameters (ADPs) of the non-hydrogen atoms) and internal motion (due to high frequency molecular vibrations, namely, bond stretching

and bending). The ADPs are now being estimated from a web server SHADE2²⁰ from where accurate estimates of the ADP values for H-atoms can be obtained, particularly for rigid molecules.²¹ It was observed that the topological estimates are affected by the level of multipole expansion used in charge density refinements with concomitant changes in electron density and Laplacian at the BCP along with the integrated atomic properties of H-atoms, namely, charge, volume, and dipole moment. An excellent article²² brings out the best refinement strategy for obtaining the best topological parameters in the absence of neutron data. This allows for refinement of H-atom positions using low angle data, elongation of X–H bond lengths to neutron values and finally supported by estimates of ADPs of H-atoms using the SHADE2 server. Finally, it has been realized that, subjected to the availability of extremely accurate experimental data, it is possible to refine the anisotropic displacement parameters for H-atoms in the case of small molecules. Such studies have been performed recently on explosives, namely, RDX and HMX, resulting in more accurate estimates of all the topological descriptors of the charge density.²³

4. APPLICATION OF ELECTRON DENSITY MEASUREMENTS

4.1. Chemical Bonding and Reactivity in Organic Molecules. The importance of electron density measurements has been most felt in the study and investigation of a topological characterization in organic molecules, in relation to a detailed elucidation of the chemical structure and the associated bonding characteristics (which includes, single, double, and triple bonds and strained rings).²⁴ This has subsequent implications on chemical reactivity²⁵ on account of variations in the derived one electron properties, namely, dipole moment, electric field gradient, and the electrostatic potential, an important topological parameter in drug-receptor interactions.²⁶ Such studies have also proved extremely significant in exploring the electron density features in the entire spectrum of interactions in intermolecular space, for example, ionic and noncovalent interactions,²⁷ namely, hydrogen bonding and halogen bonding.²⁸ An important contribution from Koch and Popelier²⁹ brings out the importance of eight necessary criteria, which must be satisfied and allows one to distinguish between interactions that are hydrogen bonded from a van der Waals interaction. The charge density and the Laplacian at the BCP are related to the total local energy density of the electrons, the contribution coming from the local potential energy density (in regions where electron density are accumulated) and local electronic kinetic energy density (in regions where density is depleted). The next development in the understanding of H-bond came from the realization of the source function, introduced by Bader and Gatti.¹⁷ The integration of this over the entire region of space gives the total electron density. The electron density at any given point in the region of the crystal comes from the contribution of every atomic basin, the contribution being the integration of the local source within the basin. This function has been applied to understand both weak and strong H-bonded systems, the value of the SF varying from negative to positive over this range.³⁰

In the past decade, electron density studies have been directed toward a quantification of topological parameters in chemical systems containing strong hydrogen bonds of the kind O–H...O (including homonuclear resonance assisted hydrogen bonds [RAHB] by variable temperature neutron diffraction and

charge density studies in tetracetylene,^{31a} and heteronuclear RAHB in 3-(aminophenylmethylene) chroman-2,4-dione and (3-(methylaminophenylmethylene)chroman-2,4-dione).^{31b} The covalent character of the strong O–H...O hydrogen bond has also been investigated by an estimation of the total local energy density $H(\text{bcp})$, this value being negative, thus indicating covalency.^{32a} This has also been verified experimentally by Compton scattering performed on Ih phase of ice^{32b} and from ab initio theoretical calculations.^{32c} These results have been extended to generate topology phase diagrams of water molecules consisting of different size clusters.^{32d} Furthermore, weak C–H...O and C–H... π interactions in coumarins³³ and π ... π interactions in cocrystals of 8-hydroxy quinoline with salicylic acid³⁴ have also been investigated. A combined experimental and theoretical study in coumarins has identified a region of overlap, wherein it was categorized that, for interactions wherein the distance between H and acceptor are less than 2.75 Å, are classified as H-bond, and above this distance are essentially van der Waals in nature.³³ The entire spectrum of different intermolecular interactions in molecular crystals were accounted for in terms of different topological estimates, namely, the electron density, Laplacian, kinetic and potential energy densities, and their variation with the interaction length. This allowed for the estimation of the energies associated with such weak interactions.^{35,36} Electron density analysis in sulfur containing compounds is rare. Such compounds on which topological analysis of the electron density have been performed primarily for the investigation of rare C–H...S interactions, who involve thio-coumarins³⁷ and 4-methyl-3-thiosemicarbazide,³⁷ establishing the fact that these are significant contributors in crystal packing. O–H...S interactions involving sulfur were characterized in *p*-cresol/MeOH and *p*-cresol/EtOH mixtures under supersonic jet conditions (gas phase) and compared with high level ab initio DFT, MP2, NBO, and AIM calculations, revealing the dispersive nature of such H-bonding.³⁸

In recent years, the importance of interactions involving halogens has been proven to contribute toward the stabilization of crystal packing. Halogen...halogen contacts are geometrically classified as type-I and type-II contacts. The origin of these interactions stems from a polar-flattening effect, which has its root in the anisotropy of electron density around the halogen atom (namely, the Williams and Nyburg model).³⁹ Both these models differ in the interpretation of the nature of the halogen...halogen interaction, the former being attractive and the latter being repulsive. Careful charge density (CD) refinements performed on hexachlorobenzene has recently established the attractive nature of type-II interactions.^{40a} Electron density analysis in three model compounds, namely, 2-chloro-3-quinoyl methanol, 2-chloro-3-hydroxy pyridine, and 2-chloro-3-chloromethyl-8-methylquinoline using high-resolution X-ray data and subsequent comparison with periodic calculations at the B3LYP/6-31G** level unambiguously brings out the fact that the *cis* and *trans* geometry in type-I interaction show decreased repulsion. The type-II geometry is attractive depending on the nature of polar flattening around the chlorine atom.^{40b} This interaction has also been quantified topologically from experimental data collected on $\text{ZnCl}_2(3,4,5\text{-trichloropyridine})_2$ and provides experimental evidence for the already existing model.^{40c} Furthermore, the relevance of C–H...Cl intermolecular interaction as a structure-directing element has been observed in CD refinements in 4-chloro-1*H*-pyrrolo[2,3-

b]pyridine. This interaction is referred to as a “weak closed shell interaction”.^{40d}

Electron density studies performed on molecules containing organic fluorine have established that C–H...F interaction is essentially a weak H-bond and that F...F interaction also falls in the regime of weak interactions.⁴¹ Disorder involving organic fluorine is a very common feature in crystal engineering⁴², and this aspect has also been modeled via careful multipole refinements in *N*-phenylpyrrole and *N*-(4-fluorophenyl)pyrrole, exhibiting static disorder in the crystal lattice.^{43a} In recent years, a new approach based on the transferability of multipole charge density parameters, for robust supramolecular synthons formed from different intra- and intermolecular interactions in crystal space, has been developed. This is called the supramolecular synthon based fragment (SBFA) approach and has been applied on high-resolution data collected for three compounds, namely, methoxybenzoic acid, acetanilide, and 4-methylbenzoic acid. The topological parameters for O–H...O carboxylic acid dimeric synthon and N–H...O amide infinite chain synthon motifs have been derived. These parameters, owing to the fact that these are obtained for robust supramolecular motifs that stabilize the crystal packing, have been used to model the charge density in 4-(acetamino)benzoic acid and 4-methylacetanilide.^{43b} An extension of this approach has now been made to explore weak C–H...O and even weaker C–H...F and C...F interactions in fluorobenzoic acids (2,3,4-position separately) crystallized with isonicotinamide. It was established that the nature of type-I F...F contacts are closed shell and exhibit features of polar flattening in the deformation density maps, and their approach in the crystal essentially results from decreased repulsion between the electron clouds.^{43c} In addition to homohalogen interactions, the extent of polarizability has been realized in molecules containing different halogens. Experimental CD studies in 2-chloro-4-fluorobenzoic acid^{43d} bring out the attractive nature associated with Cl...F contact supported by periodic theoretical calculations using CRYSTAL09. Furthermore, a systematic investigation of the electron density was performed in 5-dichloro-1,4-benzoquinone to topologically characterize the C–Cl...O=C bond. The topological values at BCP and the static DD maps clearly establish the attractive nature of such an interaction.^{43e} Other halogen bonding interactions of the type Br...N have been characterized topologically from high-resolution X-ray diffracted intensities and analyzed through Bader’s QTAIM on 1,4-dibromotetrafluorobenzene with (*E*)-1,2-bis(4-pyridyl)-ethylene or 4,4'-dipyridyl. Such calculations reveal this interaction to be at the boundary of pure and transit closed shell interaction and also accounts for the strong directional nature of halogen bonding.^{43f} An interesting QTAIM study performed on electron density data collected on cocrystals of *N*-methylpyrazine iodide with iodine molecule illustrates the amphoteric nature associated with the iodine atom. The principle stabilization comes from charge transfer, which occurs from the lone pair of I[−] to σ^* of a neutral iodine molecule and vice versa, which illustrates its amphoteric mechanism.^{43g} This allows for the existence of linear I...I–I geometries, with short distances of 3.3501 Å, and contradicts the notion that short distances can be repulsive. Halogen bonding features have also been investigated in a series of Lewis bases (ammonia, water, and hydrogen sulphide) with Lewis Acids (ClF, BrF, IF, BrCl, ICl, and IBr) and the nature of these interactions compared with Lewis acids like HF, HCl, and HBr. It was observed that halogen bonds are stronger than hydrogen bonds and that the

Laplacian distribution again indicates interaction of the lone pairs on the donor atom with the depletion region on the outermost portion of the halogen atom.^{43h}

In recent years, applications of AIM approach to study intra- and intermolecular bonding has been extended to a variety of organic compounds exhibiting different material properties. Some of these include energetic materials, namely, pentaerythritol tetranitrate crystal^{44a} and β -HMX,^{44b} to characterize the transannular N...N interaction in this class of compounds. Theoretical electron density (ED) studies in nitro containing aromatic molecules using DFT calculations and the distributed multipole analysis (DMA) establish the role of nitro groups in influencing the impact sensitivity in explosives and propellants.^{44c} Another important application is in the field of structural biology, wherein the purpose of electron density analysis is to establish a relationship between the electronic structure of the molecule and the biological function in terms of an important topological parameter, namely, the electrostatic potential (ESP) of the molecule extracted from the crystal. Detailed experimental charge density investigations have been performed on steroidal and nonsteroidal estrogens, which are important from the viewpoint of binding of the molecule with the estrogen receptor with subsequent activation or suppression of genes critical to breast cancer. Some of the important molecules in this category are estrone,^{45a} genistein,^{45b} diethylstilbestrol, and dienestrol.^{45c} The role of ESP has been realized in a comparison of the variations of this physical property in 17 β -estradiol^{45d} and 17 α -estradiol^{45e} and accounts for the variations in biological function for the former having 10 times more binding energy compared to the latter (measured experimentally in solution). The extreme significance of the ESP has also been realized in experimental CD studies performed on electrophilic compounds, which serve as model compounds for protease inhibitors (for example, consisting of aziridine ring/epoxide ring/olefin, which are electron density acceptors). The alignment of the reactive partners, for example, nucleophiles, in a chemical reaction or inhibitory activity by anchoring onto nucleophilic amino acids at the active site of the enzyme can be explored by a topological analysis of the ED and related ESP in such molecules.^{45f,g}

The role of CD research also allows one to evaluate the ED differences in compounds that exhibit polymorphism, an important phenomena that has implications in the drug industry. This has been applied to understand topological differences in polymorphs in 3-acetyl coumarin,^{46a} coumarin 314 dye,^{46b} and benzidine dihydrochloride^{46c} and to account for the variations in stability and reactivity of these polymorphs in terms of differences in intermolecular interactions and ESP.

This area of research has also been extended to understand bonding principles in 2-methyl-4-nitro-1-phenyl-1*H*-imidazole-5-carbonitrile,^{47a} 1-(2'-aminophenyl)-2-methyl-4-nitroimidazole,^{47b} Bignelli compounds (tetrahydropyrimidines),^{47c} 3,4-diamino-1,2,4-triazole (DAT) and the corresponding 5-methyl derivative (DAMT),^{47d} aminomethylphosphonic acid,^{47e} diaza-18-crown-6 dihydroazide,^{47f} and benzimidazole^{47g} and iso-indole derivatives.^{47h} Furthermore, such studies highlight chemical reactivity differences in α,β -unsaturated carbonyls and hydrazones.⁴⁷ⁱ A B...N intramolecular bond formation in 6-*tert*-butyl-2-(3',5'-difluorophenyl)-(N–B)-1,3,6,2-dioxazaborocane^{47j} has also been investigated. A detailed study to understand the thermodynamic free energy changes resulting from changes in crystal entropy between the epimers ribitol and xylitol (the former having greater entropy) signifies the

application of X-ray diffraction data to understand physicochemical properties in crystals.^{47k} The technological advancements made in this area also allow for the charge density estimates to be derived accurately for compounds that are liquids or gases at room temperature. The technique of in situ crystallization combined with collection of high-resolution X-ray data on single crystals of the compound has been applied in the case of ethylene glycol^{48a} and dinitrogen tetroxide,^{48b} which are liquids at room temperature and also in the case of ethylene oxide, a gas at room temperature.^{48c} The high strain in the 3-membered ring of this molecule is quantified in terms of the bond ellipticities of the three bonds in the ring and a high value of the electron density at the ring critical point. Related electron density studies on synchrotron data have also been performed on strained systems, namely, the [1.1.1] propellane molecule, wherein the nature of the chemical bond between two inverted bridgehead carbons (common to the three wings of the cage structure) is a topic of interest. The topological features allow the identification of so-called banana bonds outside the internuclear vectors, common in strained ring systems. In addition, cage critical points in the molecule have also been characterized, and no electron density was observed between the bridgehead carbon atoms.^{48d}

In recent years, H...H interactions have also attracted considerable interest. The two closed shell hydrogen atoms connected by a bond path, a line of maximum electron density, undergo local stabilization in the range of 1–10 kcal/mol. This aspect has been investigated in a range of chemical systems from a theoretical perspective and also from experimental electron density measurements. A recent investigation on the experimental CD analysis from high-resolution data collected at 20 K in Meldrum's Acid accounts for the fact that H...H intramolecular interactions are responsible for the stability for the boat conformation.^{49a} Such interactions are also observed in bicyclo[3.3.1]nonanes.^{49b} However, recent spectroscopic and theoretical investigations in dideuteriophenanthrene questions the validity and existence of H...H interactions in the realm of AIM approach, which oppose the traditional knowledge that such steric interactions are (Pauli) repulsive.^{49c} Subsequently, it was shown by Matta and co-workers that H...H closed shell bonding interactions stabilize the zinc(II) complex of nitrilotri-3-propanoic acid, whereby the decrease in the strain energy in the ligand is compensated by bonding H...H interactions in the complex.^{49d} These interactions have also been observed topologically in hydrides of boron and aluminum.^{49e}

4.2. Chemical Bonding in Proteins. The advancement in instrumentation (synchrotron and helium cryogenics) has resulted in the development of improved data collection protocols and methodologies, which has facilitated the determination of high quality crystal structures for large macromolecules with sufficiently better resolution (<1.0 Å).^{50a} Multipolar refinements have now been applied to investigate the total electron density distribution in such large molecules. This can lead to the evaluation of dipole moments and related one electron properties, the most important being electrostatic potential (ESP). The evaluation of such parameters allow for the identification of essential binding sites in proteins and the complementarity, which results when a drug (having its characteristic ESP) approaches the receptor site and modifies the biological function at the active site. In most cases in macromolecules, it is not possible to obtain ultrahigh-resolution, accurate data of high redundancy, which permits an evaluation of the electronic features in such crystals. A novel

approach has been developed wherein CD data has been collected on individual amino acids or small peptides (consisting of few amino acids of a known sequence),^{50b,c} and their multipole parameters (namely, the population of valence and deformation density, expansion-contraction parameter k and k') have been stored [ELMAM library: experimental library multipolar atom model]. In the case of modeling the electron density of any unknown oligopeptide, this information is transferable to amino acid residues in oligopeptides^{51a–c} and proteins.^{51d} The first CD study on a protein using ultrahigh-resolution data was collected on the crambin protein containing 46 amino acid residues and analyzed for its complete topological spectrum of the electron density.^{51e}

Another pioneering study performed on the aldose reductase consisting of 711 atoms in the active site was modeled. The CD refinements involving macromolecules are done using the software MoPro.^{52a,b} Electrostatic complementarity between the AR (protein active site) and the NADP+ (cofactor) complex reveals that the nicotinamide group in the latter having positive ESP interacts with the negative ESP at the carboxylate anion in the inhibitor IDD 594.^{53a–c} Similar charge density studies with analysis of the electrostatic interactions have been performed on Fidarestat, an inhibitor of human aldose reductase.^{53d}

A detailed investigation of the different methodologies (namely, aspherical pseudoatom formalism by Hansen–Coppens, Hirshfeld's stockholder partition, and QTAIM approach), for the purpose of transferability of the atomic multipoles in amino acids and peptides, depends upon the manner in which the total molecular density is partitioned among the individual atoms. This research revealed that the stockholder partitioning scheme is the most efficient in transfer of multipoles, followed by AIM approach, which provides meaningful comparisons for higher multipoles. However, in the case of the pseudoatom formalism, it is much less reliable for a fit of the multipolar information to the electron density.^{53e} These results are of significance from the viewpoint of modeling the electron density in proteins, an elegant study representing the transferability of ELMAM parameters for the topological analysis of the electron density in helices, the primary building blocks in macromolecules, consisting of electrostatic interactions between the N–H and C=O group. These were quantified in terms of the geometrical and energetic features associated with N...O contacts.^{53f}

4.3. Chemical Bonding in Organometallic Complexes.

An understanding of the nature of the chemical bond containing a single metal atom/multiple metal atoms with an atom (monatomic, polyatomic)/ion/organic ligand is of interest. The topological descriptors (used in organic molecules) to enable an understanding of M–L and M–M interactions in a variety of organometallic complexes (which included metal–metal bonds) are not sufficient to explain the nature of bonding in these systems^{54a} and a development of an advanced theory was necessary to elucidate the subtle electronic features associated with such chemical bonds. The Lewis model supports the concept of the 2c–2e bond, but for a vast majority of organometallic complexes (for example, dimers containing π -acid ligands, $\text{Mn}_2(\text{CO})_{10}$, $\text{Co}_2(\text{CO})_8$, in particular the ubiquitous carbonyl ligand) whereby the formal M–M bond order is one, this model proved insufficient. It was observed in electron density features obtained from experiments and theoretical calculations performed on $\text{Co}_2(\text{CO})_6(\text{AsPh}_3)_2$ that

no significant amount of electron density in the M–M region was revealed, despite the presence of BCP and BP linking the two cobalt atoms.^{54b} Similar results were obtained from theoretical deformation maps in dichromium tetracetate, and this facet was attributed to the diffuse character of metal d-orbitals.^{54c} An excellent review by Macchi, on the interpretation of chemical bonding in transition metal carbonyl clusters with inputs from both theoretical and experimental charge density studies, brings out the significance of the QTAIM approach.^{54d} To complement this work, F. Cor  s-Guzm  n and R. F. W. Bader had written another detailed review wherein they complemented QTAIM with orbital theory to understand the physics of a chemical bond. This concept was applied to the understanding of chemical bonding in $\text{Cr}(\text{CO})_6$, $\text{Fe}(\text{CO})_5$, $\text{Ni}(\text{CO})_4$, and ferrocene.^{54e} The experimental CDs in these metal carbonyls have been performed using the aspherical atom formalism (multipole model) and compared with DFT/B3LYP calculations, which show good agreement. The amount of electron density, which was back-donated from the low valent metal to the carbonyl ligand, was obtained from the values of atomic quadrupolar moments on the C atoms in all the compounds.^{54f} A topological analysis of the theoretical ED in $\text{Co}_2(\text{CO})_8$, proved the nonexistence of a BCP between the two Co atoms, at the equilibrium geometry, indicating the absence of a direct Co–Co bond.^{54g} By intuition, a bent bond character should be observed for this molecule. MO calculations to evaluate the orbital contributions to the molecular charge and energy density distributions have been performed.^{54h} Furthermore, the ED in the Co–Co region was observed to be flat, and the observed topology was sensitive to the M–M bond distance, the situation manifesting in a near catastrophic nature for the M–M interaction. For $\text{Mn}_2(\text{CO})_{10}$, a bond path for Mn–Mn bond was, however, observed.⁵⁴ⁱ This brings into question the authenticity of the heuristic 18-electron rule (effective atomic number), a number to predict the stability of different transition metal complexes (TMC). On previous occasions, the importance of the Laplacian has been used to differentiate the mode of bonding of the carbonyl group (in terms of its bridging or terminal nature) in $\text{Fe}_2(\text{CO})_9$ and $\text{Mn}_2(\text{CO})_{10}$, wherein it was concluded that, in the former, the CO behaves like a keto group, and in the latter, it retains axial symmetry. Also in accordance with the classical back bonding model, the electron density features suggest greater donation of electron charge from the metal atom to each bridging carbonyl group.^{54j} Thus, the localization of electron density in two-center M–M bonding is an approximation, and a mechanism for the quantification of the delocalization of the electron density from the M–M bond to the ligand must be considered important to rationalize the nature of bonding. In this regard, a new parameter, namely, the delocalization index $\delta(\Omega_X\Omega_Y)$ between two atomic basins *X* and *Y* (specifies the number of pairs of electrons shared between two basins), has been proposed by Stephens and Bader.¹⁸ Another classical example of interest was $\text{Fe}_3(\text{CO})_9$, consisting of a short Fe–Fe bond distance of 2.53   .^{54k} The EAN predicted a bond order of 1. MO and QTAIM analysis gave no satisfactory proof for the existence of a direct Fe–Fe bond.^{54l} By orbital partitioning of the total density,^{54m} it was established that the delocalization index $\delta(\Omega_{\text{Fe}}\Omega_{\text{Fe}})$ was 0.4. Another technique, namely, the domain averaged Fermi Hole (DAFH) by Ponc   and co-workers,^{54n,o} confirmed the results. Their studies confirmed the 3c–2e delocalized nature of Fe–Fe bonding via the

involvement of carbonyl bridging ligand, along with no evidence for M–M bonding.

A very interesting example of the existence of chemical bonding with no formal chemical bond was observed from a combined study using high-resolution X-ray data and B3LYP/DFT quantum chemical calculations, subjected to the QTAIM approach in a trimethylenemethane (TMM) complex $\text{Fe}(\eta^4\text{-C}\{\text{CH}_2\}_3)(\text{CO})_3$. The delocalized nature of the π -ligand renders the formal hapticity as four. From the charge density analysis, only one bond path was observed between the central carbon atom with the iron atom. However, the delocalization indices and the integrated source function indicate much stronger interaction with the peripheral carbon atoms of the ligand to a greater degree, the former quantity being larger in magnitude to the latter.^{55a} An extension of this study was performed on complexes of transition metals with carbocyclic rings, these being the well studied $(\eta^5\text{-C}_5\text{H}_5)\text{Mn}(\text{CO})_3$ and $(\eta^6\text{-C}_6\text{H}_6)\text{Cr}(\text{CO})_3$, having cyclopentadienyl and a benzene ring. The concept of back bonding is also prevalent in these complexes. The most important observation is that the number of BCPs observed, either from experiment or from theory, between the central iron atom with the carbon atoms of the ring may not reflect the true formal hapticity due to the presence of soft vibrational modes in these molecules, which can get activated and lead to the disappearance of predicted BCPs. This also proves the role of fluxional behavior on the nature of bonding in these systems. The dynamics associated with ring motion in these complexes results in certain topological features, for example, bond paths, to be absent.^{55b}

Charge density studies on trinuclear $\text{Co}_3(\mu_3\text{-CX}(\text{CO}))_9$ (*X* = H, Cl) have investigated the Co–CO and Co–Co interactions using the deformation density [DD] approach and a topological analysis of the electron density using the QTAIM approach.^{55c} From this approach, no (3,–1) critical point was observed, and hence, no bond path exists between the two cobalt atoms. The calculation of the delocalization index gives a value of 0.47, identical with the value obtained in the unbridged form of $\text{Co}_2(\text{CO})_8$, which possesses a M–M bond.^{54d} In continuation of the existing work, experimental and theoretical charge density studies were performed on a cobalt complex containing an alkyne group as the coordinating ligand, namely, $\text{Co}_2(\text{CO})_6(\text{HC}\equiv\text{CC}_6\text{H}_5\text{OH})$. From the QTAIM analysis, no BCP was found between the cobalt atoms, which again contradict, as predicted from the 18-e rule, the stability of the complex. The use of the integrated source function provides information about the evidence of weak Co–Co bonding. From the viewpoint of the bonding between metal and ligand, all the BCPs between Co and C could not be located, the reason being the density at Co–C and the CoC_2 fragment is comparable to each other and lesser than the residual density of $0.1 \text{ e}\text{  }^{-3}$ obtained from the multipole model. Thus, this does not permit a complete determination of all the expected critical points in a region of flat ED. The structure is close to the topological catastrophic point. Thus, in addition to a collection of high quality electron density data, deficiencies in the multipole model and subtle changes due to the crystal field can lead to altered topology for a given atomic environment.^{55d} Another study by the same group has been performed on a tetranuclear cobalt carbonyl complex, $\text{Co}_4(\text{CO})_{12}\text{PhC}\equiv\text{C-C}\equiv\text{CPh}$ to evaluate metal–metal bonds.^{55e}

It is of importance to realize that, in one example, the use of the Hansen–Coppens multipole model presented some spurious features in the topology of the electron density. This

was the case of $\text{Ru}_3(\text{CO})_{12}$ wherein short $\text{C}_{\text{ax}}\cdots\text{C}_{\text{ax}}$ contacts (axial position) with very low values of the electron density and Laplacian were present in the molecule.^{56a} Although the authors claimed in their conclusions that “these interactions cannot therefore be considered an artifact of the multipolar analysis”, it was proved by L. J. Farrugia and H. M. Senn^{56b} that this claim is incorrect and that the presence of weak intramolecular $\text{C}\cdots\text{C}$ contacts in this molecule is indeed an artifact of the multipole modeling. Extensive calculations (relativistic and nonrelativistic) gas phase DFT calculations were performed using extended basis sets along with the incorporation of dispersion corrections, but all these failed to reproduce the observed topology from the QTAIM approach. A couple of examples on charge density measurements directed toward an understanding of metal–metal bonding in iron–carbonyl clusters also testify the above-mentioned bonding features in these classes of molecules.^{56c,d}

Related studies aimed toward the understanding of M–M bond have been performed in the dinuclear borylene complex $[\{\text{Cp}(\text{CO})_2\text{Mn}\}_2(\mu\text{-B}^t\text{Bu})]$. No BCP or BP was observed for Mn–Mn bond, and the analysis of the integrated SF reveals that 50% of the density at the midpoint of the Mn–Mn region is contributed by the CO groups, while the boron decreases the ED from the midpoint. Hence, the Mn–B bond gets topological preference, and the electron density is delocalized via the boron atom.⁵⁷ The existence of BPs with the boron atom with manganese justify the fact that these serve as “privileged exchange channels”⁵⁸ and preclude the formation of a diradical, this feature being responsible for the diamagnetic nature of the complex.

In relation to the metal–metal multiple bond, a novel case where the amount of electron density between two interacting metal atoms is high was observed in an experimental CD study on the quintuply bonded complex, $\text{Cr}_2(\text{dipp})_2$ ($\text{dipp} = (\text{Ar})\text{NC}(\text{H})\text{N}(\text{Ar})$ and $\text{Ar} = 2,6\text{-i-Pr}_2\text{C}_6\text{H}_3$). The structure consisted of one σ , two π , and two δ , and these bond characteristics have been verified using the source function, Fermi hole function, MO, and NBO calculations. The observed formal bond order is 4.6 from the NBO approach.⁵⁹ A recent review by E. Matiti and M. Sola⁶⁰ provides an excellent and detailed application of the concept of delocalization in transition metal complexes along with an understanding of metal–metal bonding.

ED studies have also been extended in rhodium complexes to understand the nature of bonding, i.e., $\text{Rh}\cdots\text{C}-\text{C}$ bond in $\text{Rh}(\text{C}_7\text{H}_8)(\text{PPh}_3)\text{Cl}$ ^{61a} and related tri-*t*-butyl^{61b} and tricyclohexyl ligands^{61c} in the same complex. The role of ESP elucidates the chemical reactivity in related complexes of rhodium having COD as ligand.^{61d} Another area of interest is the investigation of agostic interactions^{62a–c} in organometallic complexes. This has also been of importance to understand chemical reactivity and organic transformations in organometallic reactions involving C–C bond activation via metal participation.

4.4. Chemical Bonding in Inorganic Solids and Metal–Organic Compounds. Electron density analysis has been extensively applied in the field of extended inorganic solids and metal–organic complexes containing TM/RE/MG elements with O/N/S/P as the principle bonding partners. An excellent review depicting the use of synchrotron radiation aimed toward the understanding of bonding, reactivity, and related physicochemical properties reveals the potential application of this area of research.^{63a} The concept of metallicity in solids has

also been explored using the QTAIM approach.^{63b} Two important solids whose CD analysis was performed are cuprite (Cu_2O)^{64a,b} and the superconductor, $\text{YBa}_2\text{Cu}_3\text{O}_{7-\delta}$.^{65a} Following the work of Zuo et al.^{65b} using convergent beam electron diffraction technique on Cu_2O , Schneider performed multipole refinements using synchrotron data,^{65c,d} and it was established that 0.5e was transferred from each of the Cu atoms to O atom in Cu_2O , and hence, bonding is ionic rather than covalent as predicted previously by Zuo et al.^{65b}

In recent years, the focus has shifted toward the characterization of M–L bonding in rare earth elements. The number of reports of CD studies in such compounds containing very heavy atoms in the structure is very few. This is mainly due to the magnitude of systematic errors due to absorption and extinction in the experimental data, which may lead to significant problems in the modeling of CD. A small crystal and use of synchrotron data can minimize these effects. One such case was the analysis of chemical bonding in the actinide system, namely, $\text{Th}(\text{S}_2\text{PMe}_2)_4$.⁶⁶ A very recent study has been performed on CsUO_2Cl_4 for topological characterization of the electron density and an understanding of the nature of bond formation in the uranyl ion $[\text{UO}_2^{2+}]$ present in this compound. Highly accurate CD data at 20 K revealed a bond order of 3 for the uranyl compound, and the charge density is shifted toward the oxygen atom in the U–O bond. It was also realized that, in addition to the valence electrons, the core electrons also play an important role in scattering, and the accuracy of their modeling depends on the quality of high-angle data.⁶⁷

There exists in the literature a wide range of homoleptic and heteroleptic transition metal complexes, which exhibit different structural, electronic, and magnetic properties. A classical example in the literature are copper complexes [general formula: $\text{Cu}_2(\text{OOCR})_4\text{L}_2$]. Their structural and magnetic properties have been explored. In this regard, charge density studies have been performed in the tetrakis- μ -(acetylsalicylate)-dicopper(II) complex using high-resolution X-ray data modeled using the multipolar model.^{68a} The nature of Cu–O bonds and Cu \cdots Cu contacts reveal that the former consists of ionic interactions, and in the latter, these interactions are weak. A related study has been performed on 3-amino-propanolato Cu(II) complexes containing coordinating anions (nitrite, nitrate, and formate).^{68b} The Cu–O and Cu–N bond is strongly covalent in the primary coordination environment. Cu–O contacts are, however, ionic with ligands. As is known from the literature, the two copper centers are antiferromagnetically coupled, but the topological analysis reveals no Cu \cdots Cu interaction. However, the value of the delocalization index $\delta(\text{Cu}-\text{Cu}')$ is low. The presence of the ring structure, analysis of *d*-orbital population, and weak Cu \cdots Cu interactions support the presence of the superexchange mechanism via the bridging oxygen atoms. A very recent detailed theoretical study using the AIM approach has been performed for the investigation of cuprophilicity in complexes containing short Cu(I)–Cu(I) contacts in the solid state. The AIM analysis reveals a BCP in most cases; these are shared interactions (ratio of $|V_{\text{c}}|/G_{\text{c}}$), and their energies are comparable to the strength of a weak hydrogen bond.^{68c} CD studies, utilizing synchrotron data, measured at helium temperatures, also find application in the understanding of antiferromagnetic ordering in coordination polymers (trinclear cobalt)^{68d} and metal–organic frameworks^{68e} (trinuclear manganese). In both cases, no existence of direct metal–metal bonding were revealed.

Theoretical DFT studies on the topology of the CD in complexes of Mn(III), Fe(III), and Co(III) with 8-hydroxy quinoline reveal that the charge depletion regions on the metal atom (at six regions) face the charge concentrated regions on the ligands in a lock and key mechanism and that the interactions with N/O donor atoms of the ligand are of a closed shell nature. The values of the delocalization index (δ_{C-C}) indicates that coordination resulted in an increase in the aromaticity of the system indicating delocalization of the electron density over the complex with noticeable increase in the strength of the C–H bonds on coordination.^{68f}

The most powerful application of CD in metal–organic systems is in understanding variations in electron density distributions in redox active complexes containing metal ions in different oxidation states in the complexes. Such molecules serve as mimics for biological processes at enzymatic sites and are important in the understanding of electron-transfer mechanisms over different metal centers. Simple electron-counting procedures are not the true representation of the electron density. Rather, the observed ED is dynamic, and the observed topology is time and space averaged over the unit cell. These features have been explored in trinuclear complexes of iron, namely, $[\text{Fe}_3\text{O}(\text{CH}_2\text{ClCOO})_6(\text{H}_2\text{O})]\cdot 3\text{H}_2\text{O}$, and the oxidized form, $[\text{Fe}_3\text{O}(\text{CH}_2\text{ClCOO})_6 - (\text{H}_2\text{O})_2(\text{CH}_2\text{ClCOO})]\cdot \text{H}_2\text{O}$ ^{68g} and also to explore spin crossover transition in $\text{Fe}(\text{btr})_2(\text{NCS})_2\cdot \text{H}_2\text{O}$; btr = bis-triazole.^{68h}

Recent studies also indicate the participation of alkaline earth metals, for example, complexes of magnesium(I) in the formation of metal–metal bonds. The nature of bonding in such complexes has been studied using high-resolution single-crystal diffraction data at 89 K on $[\text{Mg}(\text{dippnacac})]_2$, [dippnacac = $(\text{ArNCMe})_2\text{CH}$, Ar = 2,6-*i*-Pr₂C₆H₃]. CD analysis reveals a bcp, and thus, a chemical bond unambiguously exists between the magnesium atoms.^{69a} Further, theoretical calculations reveal a non-nuclear attractor, otherwise not present in a stable species. In accordance with inputs from the QTAIM approach, it was mentioned that, instead of an Mg–Mg bond, two Mg pseudoatom bonds are present.^{69b} The Laplacian values are negative indicating charge concentration in the region between the magnesium atoms (overlap of electrons in 3s orbitals) and indicative of covalent bonding. Thus, such complexes can function as reducing agents, subsequently getting oxidized to Mg(II) at the end of the chemical reaction. Experimental CD studies in another complex of magnesium, namely, $[\text{Mg}\{(\text{pz})_3\text{C}\}_2]$ (1), (pz = 3,5-dimethylpyrazolyl), reveal the closed-shell nature of the Mg–N bond. The electron density is contained in the two carbon lone-pairs, which are noncoordinating and not delocalized onto the planar pyrazoyl ring. The charge concentration was observed at the nitrogen center, and no CT took place at the metal center. Thus, Mg was concluded to exist as a dipositive cation, the driving force being the dative bond formation from N → Mg.^{69c}

Importance of CD analysis is now being applied to investigate bonding in main group elements. Recent experimental CD study and the topological properties were studied in tetraborane(10) having 14 skeletal electrons (belonging to the arachno structure). It was shown that the B–H (terminal bonds, 2c–2e) are more covalent than the B–H (bridging bonds, 3c, 2e) and that the structure is highly polarized as revealed by the interpretation from ESP. The B₄H₁₀ molecule is formally separated into B₂H₆^{4–} and two BH²⁺ fragments in the crystal.^{70a} The understanding of bonding in boranes was

extended to other related boranes, namely, two closo boranes B₁₀H₁₀^{2–} and B₁₂H₁₂^{2–} and also to account for Lewis acid–base behavior, i.e., the nature of B–N bonding in arachno boranes, namely, B₁₀H₁₂L₂; L = NH₃ and CH₃CN. The charge transfer happens via B–N dative bond formation in the latter and via H···H contacts in the former.^{70b} Another interesting case of bonding involves B–O contact. This has been investigated in $[\text{C}_{10}\text{H}_{26}\text{N}_4][\text{B}_5\text{O}_6(\text{OH})_4]_2$ by experimental and DFT calculations. It is realized that B–O has mixed covalent and ionic character. From ESP studies, it is reflected that tetrahedrally connected oxygen atoms have more negative areas of ESP compared to other trigonally coordinated oxygen atoms and other hydroxyl oxygen atoms.^{70c} A very recent ED investigation has been performed on 2-(2-pyridylimino)-2H-1,2,4-thiadiazolo[2,3-*a*]pyridine to investigate (3c–4e) interactions of the type N···S···N and compared with the related pyrimidyl system. Related molecules, which include Se and Te in place of sulfur, have been topologically studied to characterize the corresponding N···Se···N and N···Te···N interactions. It was observed that, in the case of sulfur, the bonding is a mixture of covalency and ionicity (shared shell interactions), whereas in the latter, these are closed shell interactions of charge transfer type.^{70d} Some important reports in the literature are directed toward bonding aspects in complexes of antimony containing Sb–O/N bonds,^{70e} P–M bonds,^{70f} and Ni–N bonds.^{70g}

5. CONCLUSIONS AND FUTURE PERSPECTIVES

The chemistry of the elements and related simple concepts of bonding, in terms of VSEPR theory, have been known for a long time. The research in the last two decades has not only targeted concepts related to a detailed understanding of chemical bonding in terms of a complete topological analysis of the charge density in the crystal but also on the applications of these studies to understand the role and function of solids and hence to provide a quantitative platform for structure–property correlation in solids (organic, inorganic, and organo-metallic) and macromolecules, which aims to benefit the entire scientific community at large. The focus is now shifted toward the understanding of topological features in crystalline solids formed under the application of pressure (leading to phase transitions) and variable temperature studies in compounds. Furthermore, time-resolved X-ray diffraction studies directed toward mapping of the change in dynamics of the structure and the associated electron density features is also of interest. The time required to probe such changes range from picoseconds to femtoseconds, the latter being more sensitive to monitor structural changes in solids. This results in a perturbation of the electron density distribution, and an investigation of the topology in the redistributed electron density can allow the mapping of the changes associated with events wherein phase transitions play an important role.

■ AUTHOR INFORMATION

Corresponding Author

*Fax: 0755-4092392. E-mail: dchopra@iiserb.ac.in.

Notes

The author declares no competing financial interest.

Biography



Deepak Chopra is currently working as an Assistant Professor at the Indian Institute of Science Education and Research, Bhopal, since March 2009. He completed his BSc degree from Jadavpur University, Kolkata, India, followed by an MS and Ph.D. degree at the Indian Institute of Science, Bangalore, under the guidance of Professor T. N. Guru Row in January 2007. It was further followed by postdoctoral studies at the same Institute and then moved to the University of Toledo, Ohio, USA, under the supervision of Professor Alan. A. Pinkerton. His primary interests are in the areas of weak intermolecular interactions and crystal polymorphism, electron density analysis in molecular crystals, and in situ cryocrystallization of liquids.

ACKNOWLEDGMENTS

D.C. thanks IISER Bhopal for research facilities and DST-Fast track scheme for research funding. D.C. thanks Mr. Piyush Panini and Mr. Arghyadeep Dash for the diagrams and the design for the complete layout of the cover art. D.C. also thanks the reviewers for their views on the manuscript. This review is dedicated to the memory of Professor R. F. W. Bader, who passed away on January 15, 2012, for his pioneering contributions toward the understanding of chemical bonds and the applications of quantum mechanics toward the theory of AIM.

REFERENCES

- (1) Allen, F. H. *Acta Crystallogr.* **2002**, B58, 380–388.
- (2) Koritsanszky, T. S.; Coppens, P. *Chem. Rev.* **2001**, 101, 1583–1627 and references therein.
- (3) Coppens, P. *X-ray Charge Densities and Chemical Bonding*; Oxford University Press: Oxford, U.K., 1997.
- (4) (a) Bader, R. F. W. *Atoms in Molecules. A Quantum Theory*; Clarendon Press: Oxford, U.K., 1990. (b) Popelier, P. *Atoms in Molecules: An Introduction*; Prentice Hall: Harlow, U.K., 2000.
- (5) Tsirel'son, V. G.; Ozerov, R. P. *Electron Density and Bonding in Crystals*; Institute of Physics Publishing: Bristol, U.K., 1996.
- (6) Jeffrey, G. A.; Piniella, J. F. *The Application of Charge Density Research to Chemistry and Drug Design*; NATO Science Series B: Physics; Springer: New York, 1991.
- (7) Gatti, C.; Macchi, P. *Modern Charge-Density Analysis*; Springer: New York, 2012.
- (8) Iversen, B. B.; Larsen, F. K.; Pinkerton, A. A.; Martin, A.; Darovsky, A.; Reynolds, P. A. *Inorg. Chem.* **1998**, 37, 4559–4566.
- (9) Zhurov, V. V.; Zhurova, E. A.; Chen, Y.-S.; Pinkerton, A. A. *J. Appl. Crystallogr.* **2005**, 38, 827–829.
- (10) Luger, P.; Wagner, A.; Hubschle, C. B.; Troyanov, S. I. *J. Phys. Chem. Lett.* **2005**, 109, 10177–10179.
- (11) Zhurov, V. V.; Zhurova, E. A.; Pinkerton, A. A. *J. Appl. Crystallogr.* **2008**, 41, 340–349.
- (12) (a) Hansen, N. K.; Coppens, P. *Acta Crystallogr.* **1978**, A34, 909–921. (b) Volkov, A.; Macci, P.; Farrugia, L. J.; Gatti, C.; Mallinson, P.; Richter, T.; Koritsanszky, T. *XD2006*, A computer program package for multipole refinement and topological analysis of charge densities and evaluation of intermolecular interaction energies from experimental and theoretical structure factors; University of Buffalo: Buffalo, NY, 2006.
- (13) (a) Bader, R. F. W. *Acc. Chem. Res.* **1985**, 18, 9–15. (b) Bader, R. F. W.; Essen, H. *J. Chem. Phys.* **1984**, 80, 1943–1960.
- (14) Bader, R. F. W. *J. Phys. Chem.* **1998**, A102, 7314–7323.
- (15) Stalke, D. *Chem.—Eur. J.* **2011**, 17, 9264–9278.
- (16) Becke, A. D.; Edgecombe, K. E. *J. Chem. Phys.* **1990**, 92, 5397–5404.
- (17) (a) Bader, R. F. W.; Gatti, C. *Chem. Phys. Lett.* **1998**, 287, 233–238. (b) Farrugia, L. J.; Macchi, P. *J. Phys. Chem. A* **2009**, 113, 10058–10067. (c) Gatti, C. The Source Function Descriptor As a Tool to Extract Chemical Information from Theoretical and Experimental Electron Densities. In *Structure and Bonding*; Springer: Berlin, Germany, 2010; Vol. 147, pp 193–285.
- (18) Bader, R. F. W.; Stephens, M. E. *J. Am. Chem. Soc.* **1975**, 97, 7391–7399.
- (19) (a) Desiraju, G. R. *Crystal Engineering: The Design of Organic Solids*; Elsevier: Amsterdam, The Netherlands, 1989. (b) Jeffrey, G. A.; Saenger, W. *Hydrogen Bonding in Biological Structures*; Springer: Berlin, Germany, 1991. (c) Jeffrey, G. A. *An Introduction to Hydrogen Bonding*; Oxford University Press: Oxford, U.K., 1997. (d) Scheiner, S. *Hydrogen Bonding. A Theoretical Perspective*; Oxford University Press: Oxford, U. K., 1997. (e) Desiraju, G. R.; Steiner, T. *The Weak Hydrogen Bond in Structural Chemistry and Biology*; Oxford University Press: Oxford, U.K., 1999. (f) Desiraju, G. R. *Angew. Chem., Int. Ed.* **2011**, 50, 52–59.
- (20) Madsen, A. O. *J. Appl. Crystallogr.* **2006**, 39, 757–758.
- (21) Munshi, P.; Madsen, A. O.; Spackman, M. A.; Larsen, S.; Destro, R. *Acta Crystallogr.* **2008**, A62, 465–475.
- (22) Hoser, A. A.; Dominiak, P. M.; Wozniak, K. *Acta Crystallogr.* **2009**, A65, 300–311.
- (23) Zhurov, V. V.; Zhurova, E. A.; Stash, A. I.; Pinkerton, A. A. *Acta Crystallogr.* **2011**, A67, 160–173.
- (24) Grimme, S. T. *J. Am. Chem. Soc.* **1996**, 118, 1529–1534.
- (25) Bader, R. F. W.; MacDougall, P. J. *J. Am. Chem. Soc.* **1985**, 107, 6788–6795.
- (26) Politzer, P.; Murray, J. S. *Theor. Chem. Acc.* **2002**, 108, 134–142.
- (27) Dominiak, P. M.; Makal, A.; Mallinson, P. R.; Trcinska, K.; Eilmes, J.; Grech, E.; Chruszcz, M.; Minor, W.; Wozniak, K. *Chem.—Eur. J.* **2006**, 12, 1941–1949.
- (28) Metrangola, P.; Resnati, G. Halogen Bonding: Fundamentals and Applications. In *Structure and Bonding*; Springer: Berlin, Germany, 2008; Vol. 126.
- (29) Loch, U.; Popelier, P. L. *J. Phys. Chem.* **1995**, 99, 9747–9754.
- (30) Overgaard, J.; Iversen, B. B. Charge Density Studies in Hydrogen Bond Studies. In *Structure and Bonding*; Springer: Berlin, Germany, 2010.
- (31) (a) Piccoli, P. M. B.; Koetzle, T. F.; Schultz, A. J.; Zhurova, E. A.; Stare, J.; Pinkerton, A. A.; Eckert, J.; Hadzi, D. *J. Phys. Chem. A* **2008**, 112, 6667–6677. (b) Malecka, M.; Chęcinska, L.; Rybarczyk-Pirek, A.; Morgenroth, W.; Paulmann, C. *Acta Crystallogr.* **2010**, B66, 687–695.
- (32) (a) Cremer, D.; Kraka, E. *Croat. Chem. Acta* **1984**, 57, 1250. (b) Isaacs, E. D.; Shukla, A.; Platzman, P. M.; Hamann, D. R.; Barbiellini, B.; Tulk, C. A. *Phys. Rev. Lett.* **1999**, 82, 600–603. (c) Jenkins, S.; Morrison, I. *Chem. Phys. Lett.* **2000**, 317, 97–102. (d) Jenkins, S.; Restrepo, A.; David, J.; Yin, D.; Kirk, S. R. *J. Phys. Chem. Chem. Phys.* **2011**, 13, 11644–11656.
- (33) Munshi, P.; Guru Row, T. N. *J. Phys. Chem. A* **2005**, 109, 659–672.
- (34) Nguyen, T. H.; Groundwater, P. W.; Platts, J. A.; Hibbs, D. E. *J. Phys. Chem. A* **2012**, A116, 3420–3427.
- (35) Munshi, P.; Guru Row, T. N. *CrystEngComm* **2005**, 7, 608–611.

(36) Munshi, P.; Guru Row, T. N. *Cryst. Rev.* **2005**, *11*, 199–241 and references therein.

(37) Munshi, P.; Thakur, T. S.; Guru Row, T. N.; Desiraju, G. R. *Acta Crystallogr.* **2006**, *B62*, 118–127. (b) Munshi, P.; Guru Row, T. N. *Acta Crystallogr.* **2006**, *B62*, 612–626. (c) Wolstenholme, D. J.; Weigand, J. J.; Cameron, E. M.; Cameron, T. S. *Cryst. Growth Des.* **2009**, *9*, 282–290. (d) Wolstenholme, D. J.; Weigand, J. J.; Cameron, E. M.; Cameron, T. S. *Phys. Chem. Chem. Phys.* **2008**, *10*, 3569–3577. (e) Munshi, P.; Cameron, E.; Guru Row, T. N.; Ferrara, J. D.; Cameron, T. S. *J. Phys. Chem. A* **2007**, *111*, 7888–7897. (f) Francuski, B. M.; Novakovic, S. B.; Bogdanović, G. A. *CrystEngComm* **2011**, *13*, 3580–3591.

(38) Biswal, H. S.; Shirhatti, P. R.; Wategaonkar, S. J. *Phys. Chem. A* **2010**, *114*, 6944–6955.

(39) (a) Williams, D. E.; Hsu, L. Y. *Acta Crystallogr.* **1985**, *A41*, 296–301. (b) Nyburg, S. C.; Wong-Ng, W. *Inorg. Chem.* **1979**, *18*, 2790–2791. (b) Nyburg, S. C.; Wong-Ng, W. *Proc. R. Soc. London, Ser. A* **1979**, *367*, 29–45.

(40) (a) Bui, T. T. T.; Dahaoui, S.; Lecomte, C.; Desiraju, G. R.; Espinosa, E. *Angew. Chem., Int. Ed.* **2009**, *48*, 3838–3841. (b) Hathwar, V. R.; Guru Row, T. N. *J. Phys. Chem. A* **2010**, *114*, 13434–13441. (c) Wang, R.; Dols, T.; Lehmann, C. W.; Englert, U. *Chem. Commun.* **2012**, *48*, 6830–6832. (d) Hazra, D. K.; Mukherjee, A. K.; Helliwell, M.; Mukherjee, M. *CrystEngComm* **2012**, *14*, 993–1000.

(41) Chopra, D.; Cameron, T. S.; Ferrara, J. D.; Guru Row, T. N. *J. Phys. Chem. A* **2006**, *110*, 10465–10477.

(42) Chopra, D.; Nayak, S. K.; Reddy, M. K.; Guru Row, T. N. *CrystEngComm* **2012**, *14*, 200–210.

(43) (a) Meindl, K.; Henn, J.; Kocher, N.; Leusser, D.; Zacharias, K. A.; Sheldrick, G. M.; Koritsanszky, T.; Stalke, D. *J. Phys. Chem. A* **2009**, *113*, 9684–9691. (b) Hathwar, V. R.; Thakur, T. S.; Guru Row, T. N.; Desiraju, G. R. *Cryst. Growth Des.* **2011**, *11*, 616–623. (c) Hathwar, V. R.; Thakur, T. S.; Dubey, R.; Pavan, M. S.; Guru Row, T. N.; Desiraju, G. R. *J. Phys. Chem. A* **2011**, *115*, 12852–12863. (d) Hathwar, V. R.; Guru Row, T. N. *Cryst. Growth Des.* **2011**, *11*, 1338–1346. (e) Hathwar, V. R.; Gonnade, R. G.; Munshi, P.; Bhadbhade, M. M.; Guru Row, T. N. *Cryst. Growth Des.* **2011**, *11*, 1855–1862. (f) Forni, A. *J. Phys. Chem. A* **2009**, *113*, 3403–3412. (g) Nelyubina, Y. V.; Antipin, M. Y.; Dunin, D. S.; Kotov, V. Y.; Lyssenko, K. A. *Chem. Commun.* **2010**, *46*, 5325–5327. (h) Amezaga, N. J. M.; Pamies, S. C.; Peruchena, N. M.; Sosa, G. L. *J. Phys. Chem. A* **2010**, *114*, 552–562.

(44) (a) Zhurova, E. A.; Stash, A. I.; Tsirelson, V. G.; Zhurov, V. V.; Bartashevich, E. V.; Potemkin, V. A.; Pinkerton, A. A. *J. Am. Chem. Soc.* **2006**, *128*, 14728–14734. (b) Zhurova, E. A.; Zhurov, V. V.; Pinkerton, A. A. *J. Am. Chem. Soc.* **2007**, *129*, 13887–13893. (c) Anders, G.; Borges, I. *J. Phys. Chem. A* **2011**, *115*, 9055–9068.

(45) (a) Zhurova, E. A.; Matta, C. F.; Wu, N.; Zhurov, V. V.; Pinkerton, A. A. *J. Am. Chem. Soc.* **2006**, *128*, 8849–8861. (b) Yearley, E. J.; Zhurova, E. A.; Zhurov, V. V.; Pinkerton, A. A. *J. Am. Chem. Soc.* **2007**, *129*, 15013–15021. (c) Yearley, E. J.; Zhurova, E. A.; Zhurov, V. V. *J. Mol. Struct.* **2008**, *890*, 240–248. (d) Parish, D.; Zhurova, E. A.; Kirschbaum, K.; Pinkerton, A. A. *J. Phys. Chem. B* **2006**, *110*, 26442–26447. (e) Zhurova, E. A.; Zhurov, V. V.; Chopra, D.; Stash, A. I.; Pinkerton, A. A. *J. Am. Chem. Soc.* **2009**, *131*, 17260–17269. (f) Grabowsky, S.; Pfeuffer, T.; Morgenroth, W.; Paulmann, C.; Schirmeister, T.; Luger, P. *Org. Biomol. Chem.* **2008**, *6*, 2295–2307. (g) Grabowsky, S.; Pfeuffer, T.; Chęcinska, L.; Weber, M.; Morgenroth, W.; Luger, P.; Schirmeister, T. *Eur. J. Org. Chem.* **2007**, 2759–2768.

(46) (a) Munshi, P.; Venugopala, K. N.; Jayashree, B. S.; Guru Row, T. N. *Cryst. Growth Des.* **2004**, *4*, 1105–1107. (b) Munshi, P.; Jelsch, C.; Hathwar, V. R.; Guru Row, T. N. *Cryst. Growth Des.* **2010**, *10*, 1516–1526. (c) Hoser, A. A.; Jarzemska, K. N.; Dobrzycki, L.; Gutmann, M. J.; Wozniak, K. *Cryst. Growth Des.* **2012**, *12*, 3526–3539.

(47) (a) Paul, A.; Kubicki, M.; Kubas, A.; Jelsch, C.; Fink, K.; Lecomte, C. *J. Phys. Chem. A* **2011**, *115*, 12941–12952. (b) Paul, A.; Kubicki, M.; Jelsch, C.; Durand, P.; Lecomte, C. *Acta Crystallogr.* **2011**, *B67*, 365–378. (c) Rykounov, A. A.; Stash, A. I.; Zhurov, V. V.

Zhurova, E. A.; Pinkerton, A. A.; Tsirelson, V. G. *Acta Crystallogr.* **2011**, *B67*, 425–436. (d) Konovalova, I. S.; Nelyubina, Y. V.; Lyssenko, K. A.; Paponov, B. V.; Shishkin, O. V. *J. Phys. Chem. A* **2011**, *115*, 8550–8562. (e) Janicki, R.; Starynowicz, P. *Acta Crystallogr.* **2010**, *B66*, 559–567. (f) Bushmarinov, I. S.; Nabiev, O. G.; Kostyanovsky, R. G.; Antipin, M. Y.; Lyssenko, K. A. *CrystEngComm* **2011**, *13*, 2930–2934. (g) Stephen, A. D.; Thomas, R.; Srinivasan, P.; Narayanasamy, V.; Kumaradhas, P. *J. Mol. Struct.* **2011**, *989*, 122–130. (h) Chęcinska, L.; Grabowsky, S.; Malecka, M.; Rybarczyk-Pirek, A. J.; Józwiak, A.; Paulmann, C.; Luger, P. *Acta Crystallogr.* **2011**, *B67*, 569–581. (i) Grabowsky, S.; Weber, M.; Jayatilaka, D.; Chen, Y. S.; Grabowski, M. T.; Brehme, R.; Hesse, M.; Schirmeister, T.; Luger, P. *J. Phys. Chem. A* **2011**, *115*, 12715–12732. (j) Durka, K.; Kamiński, R.; Luliński, S.; Serwatowski, J.; Woźniak, K. *Phys. Chem. Chem. Phys.* **2010**, *12*, 13126–13136. (k) Madsen, A. O.; Mattson, R.; Larsen, S. *J. Phys. Chem. A* **2011**, *115*, 7794–7804.

(48) (a) Chopra, D.; Guru Row, T. N.; Arunan, E.; Klein, R. A. *J. Mol. Struct.* **2010**, *964*, 126–133. (b) Tsirelson, V. G.; Shishkin, A. V.; Stash, A. I.; Parsons, S. *Acta Crystallogr.* **2009**, *B65*, 647–58. (c) Grabowsky, S.; Weber, M.; Buschmann, J.; Luger, P. *Acta Crystallogr.* **2008**, *B64*, 397–400. (d) Messerschmidt, M.; Scheins, S.; Grubert, L.; Pätz, M.; Szeimies, G.; Paulmann, C.; Luger, P. *Angew. Chem., Int. Ed.* **2005**, *44*, 3925–3928.

(49) (a) Chopra, D.; Zhurov, V. V.; Zhurova, E. A.; Pinkerton, A. A. *J. Org. Chem.* **2009**, *74*, 2389–2395. (b) Bushmarinov, I. S.; Fedyanin, I. V.; Lyssenko, K. A.; Lapteva, V. L.; Pisarev, S. A.; Palyulin, V. A.; Zefirov, N. S.; Antipin, M. Y. *J. Phys. Chem. A* **2011**, *115*, 12738–12745. (c) Grimme, S.; Mück-Lichtenfeld, C.; Erker, G.; Kehr, G.; Wang, H.; Beckers, H.; Willner, H. *Angew. Chem., Int. Ed.* **2009**, *48*, 2592–2595. (d) Cukrowski, L.; Matta, C. F. *Chem. Phys. Lett.* **2010**, *499*, 66–69. (e) Sirsch, P.; Clark, N. L.; Onut, L.; Burchell, R. P.; Decken, A.; McGrady, G. S.; Daoud-Aladine, A.; Gutmann, M. *J. Inorg. Chem.* **2010**, *49*, 11395–11402.

(50) (a) Schmidt, A.; Lamzin, V. S. *Curr. Opin. Struct. Biol.* **2002**, *12*, 698–703. (b) Kalinowski, R.; Dittrich, B.; Hübschle, C. B.; Paulmann, C.; Luger, P. *Acta Crystallogr.* **2007**, *B63*, 753–767. (c) Grabowsky, S.; Kalinowski, R.; Weber, M.; Forster, D.; Paulmann, C.; Luger, P. *Acta Crystallogr.* **2009**, *B65*, 488–501.

(51) (a) Pichon-Pesme, V.; Jelsch, C.; Guillot, B.; Lecomte, C. *Acta Crystallogr.* **2004**, *A60*, 204–208. (b) Pichon-Pesme, V.; Lecomte, C.; Lachekar, H. *J. Phys. Chem.* **1995**, *99*, 6242–6250. (c) Jelsch, C.; Pichon-Pesme, V.; Lecomte, C.; Aubry, A. *Acta Crystallogr.* **1998**, *D54*, 1306–1318. (d) Housset, D.; Pichon-Pesme, V.; Jelsch, C.; Benabicha, F.; Maierhofer, A.; David, S.; Fontecilla-Camps, J. C.; Lecomte, C. *Acta Crystallogr.* **2000**, *D56*, 151–160. (e) Jelsch, C.; Teeter, M. M.; Lamzin, V.; Pichon-Pesme, V.; Blessing, R. H.; Lecomte, C. *Proc. Natl. Acad. Sci. U.S.A.* **2000**, *97*, 3171–3176.

(52) (a) Guillot, B.; Viry, L.; Guillot, R.; Lecomte, C.; Jelsch, C. *J. Appl. Crystallogr.* **2001**, *34*, 214–223. (b) Jelsch, C.; Guillot, B.; Lagoutte, A.; Lecomte, C. *J. Appl. Crystallogr.* **2005**, *38*, 38–54.

(53) (a) Muzet, N.; Guillot, B.; Jelsch, C.; Howard, E.; Lecomte, C. *Proc. Natl. Acad. Sci. U.S.A.* **2003**, *100*, 8742–8747. (b) Lecomte, C.; Guillot, B.; Jelsch, C.; Podjarny, A. *Int. J. Quantum Chem.* **2005**, *101*, 624–634. (c) Guillot, B.; Lecomte, C.; Podjarny, A.; Jelsch, C. *Acta Crystallogr.* **2008**, *D64*, 567–588. (d) Fournier, B.; Bendeif, E.-E.; Guillot, B.; Podjarny, A.; Lecomte, C.; Jelsch, C. *J. Am. Chem. Soc.* **2009**, *131*, 10929–10941. (e) Woinska, M.; Dominiak, P. M. *J. Phys. Chem. A* **2012**, DOI: 10.1021/jp204010v. (f) Liebschner, D.; Jelsch, C.; Espinosa, E.; Lecomte, C.; Chabriere, E.; Guillot, B. *J. Phys. Chem. A* **2011**, *115*, 12895–12904.

(54) (a) Macchi, P. *Chimia* **2009**, *63*, 29–34. (b) Macchi, P.; Prosperpio, D. M.; Sironi, A. *J. Am. Chem. Soc.* **1998**, *120*, 13429–13435. (c) Benard, M.; Coppens, P.; DeLucia, M. L.; Stevens, E. D. *Inorg. Chem.* **1980**, *19*, 1924–1930. (d) Macchi, P.; Sironi, A. *Coord. Chem. Rev.* **2003**, *238* – 239, 383–412 and references therein. (e) Cortes-Guzman, F.; Bader, R. F. W. *Coord. Chem. Rev.* **2005**, *249*, 633–662. (f) Farrugia, L. J.; Evans, C. *J. Phys. Chem. A* **2005**, *109*, 8834–8848. (g) Low, A. A.; Kunze, K. L.; MacDougall, P. J.; Hall, M. B. *Inorg. Chem.* **1991**, *30*, 1079–1086. (h) Kluge, O.; Finger, M.;

- Reinhold, J. *Inorg. Chem.* **2005**, *44*, 6494–6496. (i) MacDougall, P. J. Ph.D. Thesis, McMaster University, 1990. (j) Bo, C.; Sarasa, J.-P.; Poblet, J.-M. *J. Phys. Chem.* **1993**, *97*, 6362–6366. (k) Cotton, F. A.; Troup, J. M. *J. Chem. Soc., Dalton Trans.* **1974**, 800. (l) Bo, C.; Sarasa, J.-P.; Poblet, J.-M. *J. Phys. Chem.* **1993**, *97*, 6362. (m) Reinhold, J.; Kluge, O.; Mealli, C. *Inorg. Chem.* **2007**, *46*, 7142. (n) Ponec, R.; Lendvay, G.; Chaves, J. J. *Comput. Chem.* **2008**, *29*, 1387. (o) Ponec, R.; Gatti, C. *Inorg. Chem.* **2009**, *48*, 11024.
- (55) (a) Farrugia, L. J.; Evans, C.; Tegel, M. *J. Phys. Chem. A* **2006**, *110*, 7952. (b) Farrugia, L. J.; Evans, C.; Lentz, D.; Roemer, M. *J. Am. Chem. Soc.* **2009**, *131*, 1251–1268. (c) Farrugia, L. J.; Evans, C. *R. Chim.* **2005**, *8*, 1566. (d) Overgaard, J.; Clausen, H. F.; Platts, J. A.; Iversen, B. B. *J. Am. Chem. Soc.* **2008**, *130*, 3834–3843. (e) Overgaard, J.; Platts, J. A.; Iversen, B. B. *Acta Crystallogr.* **2009**, *B65*, 715–723.
- (56) (a) Gervasio, G.; Marabello, D.; Bianchi, R.; Forni, A. *J. Phys. Chem. A* **2010**, *114*, 9368–9373. (b) Farrugia, L. J.; Senn, H. M. *J. Phys. Chem. A* **2012**, *116*, 738–746. (c) Farrugia, L. J.; Evans, C.; Senn, H. M.; Hänninen, M. M.; Sillanpää, R. *Organometallics* **2012**, *31*, 2559–2570. (d) Farrugia, L. J.; Senn, H. M. *J. Phys. Chem. A* **2010**, *114*, 13418–1343.
- (57) Flierler, U.; Burzler, M.; Leusser, D.; Henn, J.; Ott, H.; Braunschweig, H.; Stalke, D. *Angew. Chem., Int. Ed.* **2008**, *47*, 4321–4325.
- (58) Pendás, A. M.; Francisco, E.; Blanco, M. A.; Gatti, C. *Chem.—Eur. J.* **2007**, *13*, 9362–9371.
- (59) Wu, L. C.; Hsu, C. W.; Chuang, Y. C.; Lee, G. H.; Tsai, Y. C.; Wang, Y. J. *J. Phys. Chem.* **2011**, *115*, 12602–12615.
- (60) Matito, E.; Solà, M. *Coord. Chem. Rev.* **2009**, *253*, 647–665 and references therein.
- (61) (a) Sparkes, H. A.; Brayshaw, S. K.; Weller, A. S.; Howard, J. A. K. *Acta Crystallogr.* **2008**, *B64*, 550–557. (b) Sparkes, H. A.; Chaplin, A. B.; Weller, A. S.; Howard, J. A. K. *Acta Crystallogr.* **2010**, *B66*, 503–514. (c) Sparkes, H. A.; Krämer, T.; Brayshaw, S. K.; Green, J. C.; Weller, A. S.; Howard, J. A. *Dalton Trans.* **2011**, 40, 10708–10718. (d) Bendeif, E. E.; Matta, C. F.; Stradiotto, M.; Fertey, P.; Lecomte, C. *Inorg. Chem.* **2012**, *51*, 3754–3769.
- (62) (a) Scherer, W.; Wolstenholme, D. J.; Herz, V.; Eickerling, G.; Bruck, A.; Benndorf, P.; Roesky, P. W. *Angew. Chem., Int. Ed.* **2010**, *49*, 2242–2246. (b) Scheins, S.; Messerschmidt, M.; Gembicky, M.; Pitak, M.; Volkov, A.; Coppens, P.; Harvey, B. G.; Turpin, G. C.; Arif, A. M.; Ernst, R. D. *J. Am. Chem. Soc.* **2009**, *131*, 6154–6160. (c) Scherer, W.; Herz, V.; Hauf, C. On the Nature of β -Agostic Interactions: A Comparison Between the Molecular Orbital and Charge Density Picture. In *Structure and Bonding*; Springer: Berlin, Germany, 2012.
- (63) (a) Coppens, P.; Iversen, B. B.; Larsen, F. K. *Coord. Chem. Rev.* **2005**, *249*, 179–195 and references therein. (b) Jenkins, S.; Ayers, P. W.; Kirk, S. R.; Mori-Sánchez, P.; Pendás, A. M. *Chem. Phys. Lett.* **2009**, *471*, 174–177.
- (64) (a) Restori, R.; Schwarzenbach, D. *Acta Crystallogr.* **1986**, *B42*, 201. (b) Kirfel, A.; Eichhorn, K. *Acta Crystallogr.* **1990**, *A46*, 271.
- (65) (a) Lippmann, T.; Blaha, P.; Andersen, N. H.; Poulsen, H. F.; Wolf, T.; Schneider, J. R.; Schwarz, K. H. *Acta Crystallogr.* **2003**, *A59*, 437–451. (b) Zuo, J. M.; Kim, M.; O’Keefe, M.; Spence, J. C. H. *Nature* **1999**, *401*, 49–52. (c) Lippmann, T.; Schneider, J. R. *J. Appl. Crystallogr.* **2000**, *33*, 156. (d) Lippmann, T.; Schneider, J. R. *Acta Crystallogr.* **2000**, *A56*, 575.
- (66) (a) Iversen, B. B.; Larsen, F. K.; Pinkerton, A. A.; Martin, A.; Darovsky, A.; Reynolds, P. A. *Inorg. Chem.* **1998**, *37*, 4559–4566. (b) Iversen, B. B.; Larsen, F. K.; Pinkerton, A. A.; Martin, A.; Darovsky, A.; Reynolds, P. A. *Acta Crystallogr.* **1999**, *B55*, 363–374.
- (67) (a) Zhurov, V. V.; Zhurova, E. A.; Pinkerton, A. A. *Inorg. Chem.* **2011**, *50*, 6330–6333. (b) Zhurov, V. V.; Zhurova, E. A.; Stash, A. I.; Pinkerton, A. A. *J. Phys. Chem. A* **2011**, *115*, 13016–13023.
- (68) (a) Bouhmaida, N.; Méndez-Rojas, M. A.; Pérez-Benítez, A.; Merino, G.; Fraisse, B.; Ghermani, N. E. *Inorg. Chem.* **2010**, *49*, 6443–6452. (b) Farrugia, L. J.; Middlemiss, D. S.; Sillanpää, R.; Seppälä, P. *J. Phys. Chem. A* **2008**, *112*, 9050–9067. (c) Dinda, S.; Samuelson, A. G. *Chem.—Eur. J.* **2012**, *18*, 3032–3042. (d) Clausen, H. F.; Overgaard, J.; Chen, Y. S.; Iversen, B. B. *J. Am. Chem. Soc.* **2008**, *130*, 7988–7996.
- (e) Poulsen, R. D.; Bentien, A.; Chevalier, M.; Iversen, B. B. *J. Am. Chem. Soc.* **2005**, *127*, 9156–9166. (f) Murgich, J.; Franco, H. J. *J. Phys. Chem. A* **2009**, *113*, 5205–5211. (g) Overgaard, J.; Larsen, F. K.; Schiøtt, B.; Iversen, B. B. *J. Am. Chem. Soc.* **2003**, *125*, 11088–11099. (h) Legrand, V.; Pillet, S.; Souhassou, M.; Lugan, N.; Lecomte, C. *J. Am. Chem. Soc.* **2006**, *128*, 13921–13931.
- (69) (a) Overgaard, J.; Jones, C.; Stasch, A.; Iversen, B. B. *J. Am. Chem. Soc.* **2009**, *131*, 4208–4209. (b) Platts, J. A.; Overgaard, J.; Jones, C.; Iversen, B. B.; Stasch, A. *J. Phys. Chem. A* **2011**, *115*, 194–200. (c) Kratzert, D.; Leusser, D.; Stern, D.; Meyer, J.; Breher, F.; Stalke, D. *Chem. Commun.* **2011**, 47, 2931–2933.
- (70) (a) Forster, D.; Hubschle, C. B.; Luger, P.; Hugle, T.; Lentz, D. *Inorg. Chem.* **2008**, *47*, 1874–1876. (b) Mebs, S.; Kalinowski, R.; Grabowsky, S.; Förster, D.; Kickbusch, R.; Justus, E.; Morgenroth, W.; Paulmann, C.; Luger, P.; Gabel, D.; Lentz, D. *J. Phys. Chem. A* **2011**, *115*, 1385–1395. (c) Hathwar, V. R.; Paul, A. K.; Natarajan, S.; Guru Row, T. N. *J. Phys. Chem. A* **2011**, *115*, 12818–12825. (d) Nakanishi, W.; Hayashi, S.; Pitak, M. B.; Hursthouse, M. B.; Coles, S. J. *J. Phys. Chem. A* **2011**, *115*, 11775–11787. (e) Fukin, G. K.; Baranov, E. V.; Jelsch, C.; Guillot, B.; Poddelsky, A. I.; Cherkasov, V. K.; Abakumov, G. A. *J. Phys. Chem. A* **2011**, *115*, 8271–8281. (f) Henn, J.; Meindl, K.; Oechsner, A.; Schwab, G.; Koritsanszky, T.; Stalke, D. *Angew. Chem., Int. Ed.* **2010**, *49*, 2422–2426. (g) Domagala, S.; Daszkiewicz, B. K.; Straver, L.; Woźniak, K. *Inorg. Chem.* **2009**, *48*, 4010–4020.