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The n → π* interaction in metal complexes†

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We report here, for the first time, the existence of n → π* interactions in transition metal complexes containing carbonyl ligands. This interaction has been observed to be surprisingly abundant and to stabilize precise molecular conformations that maximize the overlap between the donor and acceptor orbitals.

Noncovalent interactions are key in numerous chemical and biological processes.[1–4] A particular type of weak interaction, called the n → π* interaction, has attracted much interest in recent years due to its unambiguous contribution to protein structure, but also because it dictates the conformation of a plethora of organic molecules.[5,6] In a recent report, Das *et al.* have given further experimental evidence for an n → π* interaction in phenyl formate.[7] According to the same authors, n → π* interactions can be roughly divided into two groups, n → π*Am (amide) and n → π*Ar (aromatic).[6] One of the most common n → π*Am interactions is that involving two carbonyl groups with a C=O···C=O distance shorter than the sum of the van der Waals radii (3.27 Å).[8] Such carbonyl–carbonyl interaction has the origin in the overlap of an oxygen lone pair (n) and a carbonyl empty antibonding orbital (π*) that involves some degree of electron delocalization of the first into the second.[9] The energy release resulting from this orbital mixing (approximately 0.27 kcal mol^{-1})[5] makes the interaction attractive. A great effort to unravel the nature and to understand the signatures of the n → π* interaction has been done by Raines group and others, who have extensively investigated its presence in lactones,[10] collagen,[11] prolines,[12] aminobutyric acid,[13] aspirin[14] and peptoids.[15]

However, carbonyl groups are not confined to organic compounds since they are commonly found acting as neutral ligands in transition metal complexes. A carbonyl ligand has

a set of two empty π* orbitals that can, *a priori*, act as acceptors of electron density. In fact, carbonyl complexes have been widely used as electrophiles in catalysis.[16,17] For instance, in Pd-catalyzed carbonylation reactions, a carbonyl can be attacked by an amine or alcohol to form an amide or ester group.[18] Therefore, one could expect that inorganic carbonyls can participate in a n → π* interaction similarly to their organic analogues do. Here, by means of a combined structural and theoretical analysis, we show that carbonyl···carbonyl short contacts are in fact ubiquitous in metal complexes. Furthermore, behind such contacts there is an attractive interaction based on the electron delocalization of a lone pair of one carbonyl in the empty orbitals of the other, giving place to a n → π* interaction. These findings extend the realm of the n → π* interaction beyond the organic world and open the possibility of using it in metal complex design.

Within a metal complex, the donor group must have certain mobility to engage in the n → π* interaction, excluding thus another carbonyl ligand and pointing to candidates among more structurally complex ligands. A quick survey reveals that 3.5% of all crystal structures found in the Cambridge Structural Database (CSD)[19] containing at least one metal–CO (terminal ligand) and one non-metal–CO moieties present intramolecular Metal–C≡O···C=O(non-metal) contacts shorter than the sum of the van der Waals radii ($\sum r_{vdW} = 3.27$ Å). These contacts do not show any marked directionality and only a few distances are shorter than 3 Å (see Fig. S1 in the ESI†), which is consistent with the low mobility of carbonyl ligands directly attached to the metal centre. If one looks for short non-metal–C≡O···C≡O(metal) contacts, the percentage rises to 22.6%. Moreover, such contacts show a clear directionality with an O···C=O angle in the range 90–100° (Fig. 1A), close to the Burgi–Dunitz trajectory (O···C=O angle = 107°), which is characteristic of the n → π* interaction.[20,21] Here, the presence of the metal atom, arranged linearly with the acceptor carbonyl, involves either a ligand (*e.g.* in octahedral complexes) or a set of occupied orbitals (*e.g.* in square-planar complexes) in the region around approach angles of 107°, precluding in this way O···C≡O angles larger than 100–105°. Moreover, according to the Burgi–Dunitz trajectory,

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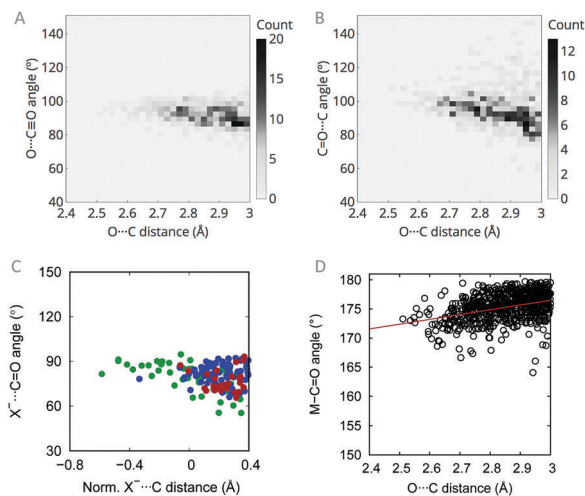
Fig. 1 Heat maps of the (A) $O{\cdots}C{\equiv}O$ and (B) $C{\equiv}O{\cdots}C$ angles as a function of the intramolecular $O{\cdots}C$ contact distance in contacts of the type non-metal$-C{\equiv}O{\cdots}C{\equiv}O$(metal), (C) $X^-{\cdots}C{\equiv}O$ angle as a function of the $X^-{\cdots}C$ distance (X = Cl, Br, I; green, blue and red points, respectively) and (D) variation of the $M-C{\equiv}O$ angle with the interaction distance (the red line is a linear regression given only as a guide to the eyes; $R^2 = 0.07$).

$O{\cdots}C{\equiv}O$ angles around $100°$ should maximize the overlap between the donor lone pair and the acceptor empty π^* orbitals in transition metal complexes. Previous studies of $C{\equiv}O{\cdots}C{\equiv}O$ contacts in organic molecules have shown the absence of a trend in the dihedral angle between the two interacting carbonyl groups,[9] a behaviour that has been reproduced here in the context of carbonyl complexes. In the present case, however, I have observed some degree of dependence between the $C{\equiv}O{\cdots}C$ angle and the contact distance (Fig. 1B). However, the angle values are more variable than for the $O{\cdots}C{\equiv}O$ (Fig. 1A) and, moreover, they can be imposed by the coordination geometries associated to different metal complexes.

Previous studies have extensively investigated the nature of $C{\equiv}O{\cdots}C{\equiv}O$ interactions demonstrating that a purely electrostatic picture cannot explain experimental and computational observations in protein residues.[5] Inspired by Raines and co-workers, who analysed the origin of intimate interactions with carbonyl groups in organic compounds in terms of geometrical parameters,[9] I have searched the CSD for short contacts where the donor is a halide anion ($X^-{\cdots}C{\equiv}O$; X = F, Cl, Br, I) to further test whether carbonyl··carbonyl interactions in transition metal complexes are of electrostatic dipolar nature. In this case, there is no dipole associated to the donor and, thus, if the interaction is dipolar one should not expect any directional short contact. Remarkably, it has been found for halides the same angular occurrence as that found when the donor is a carbonyl (Fig. 1C). This finding reinforces the orbital hypothesis since it indicates that a dipole is not needed in the nucleophile in order to establish an interaction.

Another signature of the n → π^* interaction is the pyramidalization of the $R_2C{\equiv}O$ moiety. Numerous studies have shown that short $O{\cdots}C$ distances along the Burgi–Dunitz trajectory involve the displacement of the electrophilic carbon out of the $R_2C{\equiv}O$ plane,

approaching in this way the acceptor to the donor in an incipient evolution toward an sp^3 hybridization as a consequence of the orbital mixing.[22] When studying terminal carbonyl ligands, one cannot analyse such pyramidalization angle, but a similar linearity loss in the $M-C{\equiv}O$ framework could be expected for short $O{\cdots}C$ distances. Interestingly, a survey of the CSD discloses such dependence (Fig. 1D). While $M-C{\equiv}O$ angles are between 175 and $180°$ for $O{\cdots}C$ distances larger than 2.8 Å, for shorter distances the angles approach the $170–175°$ region. This change in the angle could also be due to a geometrical rearrangement to avoid repulsion between the lone pair donor orbital and the occupied π orbital of the carbonyl ligand, which also leads to a maximization of the n/π^* orbital overlap.[23] In any case, the observed angle variation, in one direction or the other, points toward some orbital involvement in the carbonyl··carbonyl short contact.

Carbonyl ligands are neutral but they also shown some degree of polarization, presenting a region of charge depletion in the carbon atom while the terminal oxygen shows a charge accumulation. Accordingly, an electrostatic contribution to the carbonyl··carbonyl interaction could be expected accompanying the orbital delocalization. In the case of anionic compounds, this possible $O^{\delta-}{\cdots}C^{\delta+}$ interaction should be diminished, leaving the n → π^* mixing as the most important stabilizing factor. Remarkably, a nice example of an intimate carbonyl interaction within an anionic complex has been found in the crystal structure of a Pt(II) square-planar complex[24] (Fig. 2A). In that crystal, there is an intramolecular $C{\equiv}O{\cdots}C{\equiv}O$ contact at 2.87 Å, considerably shorter that the sum of the vdW radii. The representation of the molecular electrostatic potential of the anionic complex shows a negative surface around the whole molecule, but it is known that the presence of countercations in the crystal structure can significantly modify the MEP picture of the anionic complex.[25] Moreover, the natural charge (NPA) at the carbonyl C atom is still positive, which allows some degree of electrostatic interaction with an electron-rich donor. An NBO analysis shows a stabilizing interaction involving a lone-pair of the donor O and an empty antibonding π orbital of the acceptor carbonyl (Fig. 2B) with an associated energy of 0.58 kcal mol^{-1}. Notably, this energy falls within the range of previous n → π^* interactions found in organic compounds.[5,6]

Carbonyl··carbonyl short contacts are also found in neutral metal complexes. In Fig. 3A, we represent the short $O{\cdots}C$
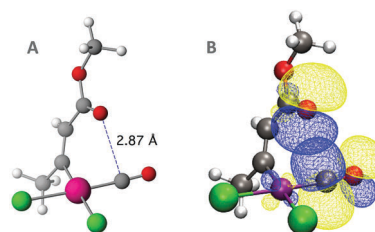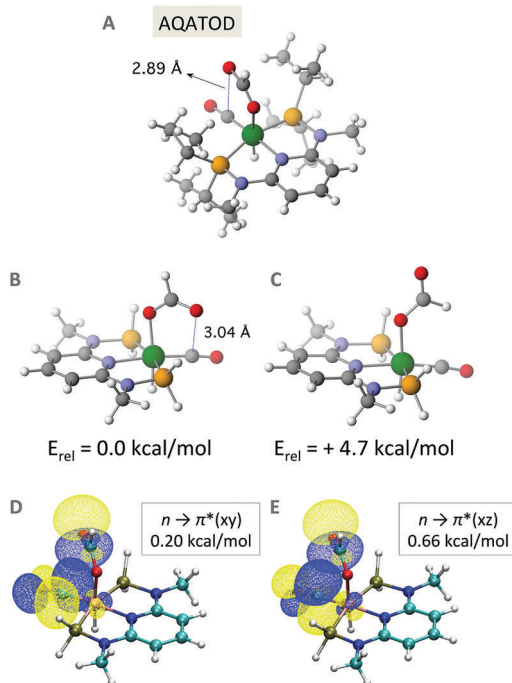

Fig. 2 (A) Short carbonyl··carbonyl contact found in the crystal structure of bis(triphenylphosphine)iminium carbonyl-dichloro-(3-(methoxycarbonyl)-prop-2-en-2-yl)-platinum(II)[24] (CSD refcode: GEMLUF) and (B) NBO results representing the overlap between the carbonyl n and π^* orbitals.

contact (2.89 Å) between a formate and a carbonyl ligand in a Fe(II) complex.[26]

To further investigate intimate carbonyl interactions, a model system based on such molecule has been created. The isopropyl groups on the phosphines have been eliminated to avoid possible C–H···O interactions and allow free rotation of the upper formate. After full geometry optimization, the short O···C contact is still present at 3.04 Å (Fig. 3B). I have also built the model isomer in which there is no possibility of O···C contact by rotating 180° the Fe–O–C≡O dihedral (Fig. 3C). Interestingly, the zero-point corrected relative energies of the two isomers show that the interacting one is 4.7 kcal mol^{-1} more stable than the non-interacting one. It seems thus clear that such energy stabilization comes from the presence of the carbonyl···carbonyl short contact. Furthermore, its attractive nature is associated with donor–acceptor orbital interactions between lone pair and empty π* orbitals (Fig. 3D and E), i.e. a n → π* interaction. Here, conversely to what is observed in proteins and organic compounds, two perpendicular empty π* orbitals can participate as acceptors in the interaction. In fact, there are also two lone pairs involved in the interaction, one with more p and the other with more s character. The four interactions derived from the four orbitals mixing account for a total energy release of 1.08 kcal mol^{-1} according to the NBO analysis. From a geometrical point of view, the relative position of the two carbonyl groups (C–Fe–O–C dihedral = 40.5°) seems

Table 1 Geometrical parameters and second order perturbation energies of the n → π* interaction for several modifications of the model complex in Fig. 3B. Energies are given in kcal mol^{-1}

Int. unit	Non-int. unit	Norm. $d_{O\cdots C}$ (Å)	O···C≡O angle (°)	M–C≡O angle (°)	$E^{(2)}$ $n_s \to \pi^*$	$E^{(2)}$ $n_p \to \pi^*$
≡O	–H	−0.23	104.8	175.4	0.22	0.86
≡S	–H	−0.12	101.7	171.9	0.26	1.53
≡O	–CF₃	−0.19	104.1	175.2	0.19	0.68
≡O	–CMe₃	−0.33	103.6	175.0	0.33	1.22

to maximize the overlap of the two lone pairs (s and p) with the two π* (xy and xz) orbitals. Note that in the case of a dipolar interaction such deviation of the dihedral angle from 0° should, in principle, not be observed.

I have next analyzed substitution effects both in the interacting and the non-interacting units of the formate ligand of the model molecule. The results are shown in Table 1. The first observation is that replacing the oxygen donor with sulphur reinforces the n → π* interaction, increasing the associated energy in 0.71 kcal mol^{-1}. The enhancing effect of including a better donor, but a poorer dipole, as S can be considered as evidence of the orbital nature of the n → π* interaction.[5] The presence of S also leads to the most dramatic change in the M–C≡O angle (171.9°), which could be due to the increased steric demand of the thiocarbonyl group. If we keep the same donor atom (O) and we modify the non-interacting unit, some changes are also observed. The presence of an electron-withdrawing group as CF₃ attached to the donor carbonyl reduces its capability as a nucleophile,[10] which is reflected in a decrease on the energy of the interaction (0.21 kcal mol^{-1} weaker). Conversely, attaching an electron-donor group as tert-butyl reinforces the n → π* interaction.

The geometry of the complex is also affected by the substituents at the non-interacting group. Remarkably, there is a nice linear correlation between the donor–acceptor (O···C) distance and the energy release due to the n → π* interaction (see Fig. S2 in the ESI†). For C≡O donors, the interaction distances are between 0.19 and 0.33 Å shorter than the sum of the vdW radii. In the case of the sulphur (C≡S donor) the contact distance is only 0.12 Å shorter than the sum of the vdW radii, which could be attributed to the larger size of S orbitals and the consequent Pauli repulsion between the lone pair and the filled π orbital of the acceptor carbonyl.[23] It is worth noting that all calculated donor···C≡O angles (101–105°) are very close to the Burgi–Dunitz trajectory and in good agreement with the previous structural analysis.

Summarizing, it has been reported here, for the first time, the existence of intramolecular n → π* interactions in transition metal complexes. These interactions are ubiquitous, stronger than similar ones in proteins and can determine the internal conformation of carbonyl complexes. It has also been shown that the interaction strength can be modulated by modification of the substituents attached to the donor carbonyl. These findings might have multiple consequences since metal complexes are important as molecular magnets, spin crossover systems or catalysts. For example, one of the Fe(II) complexes studied here (Fig. 3A),

Fig. 3 (A) Short carbonyl···carbonyl contact found in the crystal structure of carbonyl-(formato)-hydrido-(N,N′-(pyridine-2,6-diyl)bis(P,P-diisopropyl-N-methyl(phosphinous amide)))-iron (CSD refcode: AQATOD),[26] (B and C) optimized geometries of the two isomers of the model system, and (D and E) NBO results showing the overlap between the p-type lone pair orbital of the donor carbonyl and the two π* empty orbitals of the acceptor carbonyl ligand.

which is stabilized by a n $\rightarrow$ π^* interaction, is a crucial intermediate in the catalytic hydrogenation of CO_2.[26] Moreover, I anticipate that n $\rightarrow$ π^* interactions in metal compounds are not confined to intramolecular contacts, and intermolecular interactions might also play a role in the formation of solid-state structures. Future research could be directed to other common ligands similar to carbonyl as cyano and nitrosyl.

Conflicts of interest

There are no conflicts to declare.

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