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Review

Recent advances in acylpyrazolone metal complexes and their potential applications

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Contents

Abbreviations: Me, methyl; Et, ethyl; Pr, propyl; *i*Pr, *iso*-propyl; Bu, butyl; *t*Bu, *tert*-butyl; Pe, pentyl; *n*Pe, neopentyl; He, hexyl; Cp, cyclopentyl; EtCp, ethylcyclopentane; Cy, cyclohexyl; Ph, phenyl; Bn, benzyl; Biph, biphenyl; F5Ph, pentafluorophenyl; CHPh2, diphenylmethyl; Pd, pentadecyl; Hd, heptadecyl; 1naph, 1-naphthyl; 2naph, 2-naphthyl; py, pyridin-2-yl; pyCOOH, 6-carboxylic acid-2-pyridinyl; fur, 2-furyl; thi, 2-thienyl; norb, 5-bicyclo[2.2.1]hept-5-en-2-yl; AD, adamantyl; Ph2OH, 2-hydroxyphenyl; Ph4F, 4-fluorophenyl; Ph4Cl, 4-chlorophenyl; Ph3Cl, 3-chlorophenyl; Ph4Br, 4-bromophenyl; Ph4I, 4-iodophenyl; Ph4Me, 4-methylphenyl; Ph4NMe2, 4-dimethylaminophenyl; Ph4CN, 4-cyanophenyl; CF3, trifluoromethyl; Ph4CF3, 4-trifluoromethylphenyl; CF2CF3, pentafluoroethyl; Ph4*t*Bu, 4-*tert*-butylphenyl; Ph4NO2, 4-nitrophenyl; dme, 1,2-dimethoxyethane; thf, tetrahydrofurane; dmf, dimethylformamide; OAc, acetate; tetraglyme, 2,5,8,11,14-pentaoxapentadecane; tmeda, *N,N,N′,N′*-tetramethylethylenediamine; pmdien, *N,N,N′,N″,N‴*-pentamethyldiethylenetriamine; Cp*, pentamethylcyclopentadienyl; phen, 1,10-phenanthroline; bipy, 2,2′-bipyridine; tpq, 2-(thiophen-2-yl)quinolone; ppy, 2-phenylpyridine; dbzm, dibenzoylmethane; dfppy, (2,4-difluoro)phenylpyridine; dmso, dimethylsulphoxide; dpephos, bis[2-(diphenylphosphino)-pheny]ether; saph, salicylidene-*o*-aminophenol; DCJTB, 4-(dicyanomethylene)-2-*tert*butyl-6(1,1,7,7,-tetramethyljulolidyl-9-enyl)-4*H*-pyran; aac, N-phthaloyl aminoacids; acac, acetylacetone; bzac, benzoylacetone; TPPO, triphenylphosphine; dppmO_2, bis(diphenylphosphino)methane oxide; dppeO_2, bis(diphenylphosphino)ethane oxide; dpppO_2, bis(diphenylphosphino)propane oxide; dppbO_2, bis(diphenylphosphino)butane oxide; pyphenCN, pyrazino[2,3-*f*][1,10]phenanthroline-2,3-dicarbonitrile; 4,4′-Me_2bipy, 4,4′-dimethyl-2,20-bipyridyne; DPPOC, 9-(4-tert-butylphenyl)-3,6-bis(diphenylphosphineoxide)-carbazole; batophen, 4,7-diphenyl-1,10-phenanthroline; DB18C6, dibenzo-18-crown-6; DEDPU, N,N′-diethyl-N,N′-diphenylurea; DPDPU, N,N′-dipropyl-N,N′-diphenylurea; DBSOB, 1,4-di(butylsulfinyl)butane.

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ABSTRACT

This review is aimed at updating the current advance of metal complexes bearing acylpyrazolonate ligands. Novel synthetic procedures for acylpyrazolones are reported together with a survey of the ligands biological properties. All the literature since 2005 on metal complexes (main group, transition, lanthanide and actinide metals) containing acylpyrazolones is reported together with a discussion on their main structural features and field of potential applications.

1. Introduction

β-Diketones and related ligands have attracted the interest of researchers since the dawn of coordination chemistry, with the preparation of acetylacetone first described by Claisen more than 100 years ago [1], and continue to be used as ligands of choice for the synthesis of metal complexes that find application in a number of fields [2]. Much efforts have been devoted to the preparation and characterization of functionalized β-diketones suitable to finely modulate the physico-chemical features of the corresponding metal complexes, for example volatility and thermal stability sufficient to employ them as molecular precursors in chemical vapour deposition (CVD) techniques, or luminescence in view of potential application in the fabrication of polymer light-emitting diodes for low-cost, full-color, flat-panel displays, or even magnetic and electronic properties of metal β-diketonates as liquid crystal phases. But transition- and lanthanide-metal derivatives also display interesting catalytic features, where the β-diketonates are important spectator donors for metal-intermediate species involved in a number of organic reactions, and find increasing interest as supramolecular assemblies in material chemistry.

Besides classical β-diketones, an interesting functionalization has been the fusion of a pyrazole ring to the chelating arm, affording a novel family of enolizable ligands, named 4-acyl-5-pyrazolones, the first synthesis of such molecules being reported at the end of the XIX century [3], even if only in 1959 Jensen published an advantageous method of preparation of 1-phenyl-3-methyl-4-acylpyrazol-5-ones [4]. These ligands have been used for a long time as convenient metal extractants or chelating reagents in the spectroscopic determination of metals in traces, largely used in analytical chemistry for determination and isolation of almost all metal ions, due to high extracting ability of acylpyrazolonates, lower pK_a values in comparison with conventional β-dicarbonyl compounds, great separation power, intense color of the complex extracts and low-solubility of the complexes in some solvents [5]. The interesting feature of this family of molecules with respect to classical β-diketones, stemming in the presence of the pyrazole ring, is also related to the evidence that ccompounds containing pyrazole functionality exhibit anti-inflammatory and analgesic activity [6].

In 2005 we reviewed the most important synthetic routes of this family of ligands and their coordination chemistry toward many metal ions, from main group to transition, lanthanide and actinide metals and relevant applications of their metal complexes [7]. After ten years we have decided to update the knowledge in this field, because many other papers have appeared in the last decade, dealing on acylpyrazolone ligands and their metal complexes, with novel potential applications and future perspectives.

2. Ligands synthesis, structure and substituents

Following previous review [7], we will limit the discussion on the coordination chemistry of 1-R^1-3-R^2-4-R^3(C=O)-pyrazol-5-one proligands (Fig. 1), here indicated as HQ in general, where H is an enolizable proton.

There exist many variations in this class of molecules, regarding mainly the donor atoms in the chelating ring, i.e. a sulphur or a nitrogen atom at the place of one or both oxygen atoms of chain and pyrazole carbonyls, and they have been reviewed by Casas some years ago [8]. Here we will use the same symbolism previously proposed: symbols up to right of Q indicate the substituents R^1, R^2 and R^3. However, generally R^1 = Ph, R^2 = Me, so that in this case only R^3 will be indicated, i.e. HQ^{tBu} means R^1 = Ph, R^2 = Me, R^3 = *t*Bu (Fig. 2a). By contrast, when $R^1 \neq$ Ph, R^2 = Me, both R^1 and R^3 will be indicated up to right of Q, i.e. $HQ^{Me,Ph}$ means R^1 = Me, R^2 = Me, R^3 = Ph (Fig. 2b). Finally, only when $R^1 \neq$ Ph and $R^2 \neq$ Me, all R^1, R^2, R^3 groups will be indicated, i.e. $HQ^{Me,Ph,Me}$ means R^1 = Me, R^2 = Ph, R^3 = Me (Fig. 2c).

The tautomerism of 4-acylpyrazolones (Fig. 3) has been the subject of various studies: in solution a fast (relative to the NMR timescale) interconversion of OH and NH forms gives rise to averaged sets of signals [9]. The chelated hydroxy forms A, B, E and F are predominant in $CDCl_3$ or C_6D_6, and mixtures of OH and NH tautomers are present in the more-polar [D_6]DMSO. In the solid state, some unambiguous results have been obtained by single-crystal X-ray studies showing HQ proligands, crystallized from chloroform, in the enol form B [10], while the amino diketonic form C, stabilized by an extensive network of intermolecular N—H···O bonding, was confirmed from re-crystallization in polar solvents like methanol [10a,b,11]. ^{13}C and ^{15}N CPMAS spectra suggest the zwitterionic structure H for $HQ^{py,CF3}$ (Fig. 3) [12].

The synthesis of HQ is based on direct acylation of 5-pyrazolones with acyl chlorides or anhydrides in the presence of calcium hydroxide in dioxane or thf at reflux [4]. Subsequent treatment with acid aqueous solution affords the HQ in high yield as a solid powder generally insoluble in water, apart few examples such as $HQ^{Me,Me}$, which displays a quite good solubility in water and must be isolated by extraction with dichloromethane [7]. Concerning the use of calcium hydroxide, Kurteva have proved that calcium hydroxide

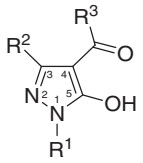

Fig. 1. Generic structure for acylpyrazolones.

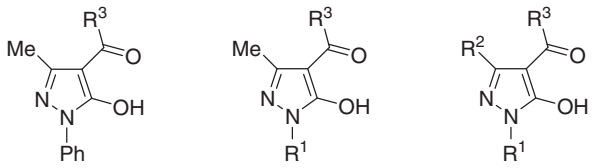

Fig. 2. Symbolism used in this review for the acylpyrazolones.