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## Shapeshifting xantphos

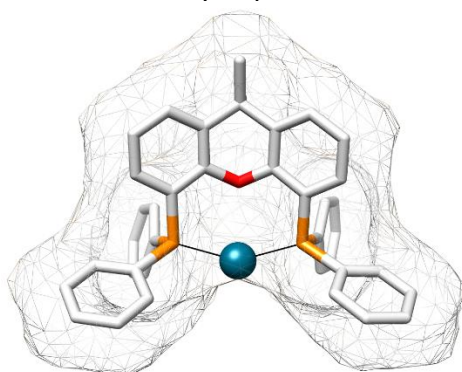
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Catalysis plays an ubiquitous role in our daily lives — it is involved in the production of over 80% of all manufactured products ranging from polymers, textiles, and fuels to fine-chemicals, such as agrochemicals and pharmaceuticals<sup>1</sup>. Notable developments in catalysis have been recognized at least 17 times by the Nobel Foundation over the years, including five Nobel Prizes in the 21<sup>st</sup> century, highlighting the continuous importance of this field<sup>2</sup>.

Among different types of strategies, transition-metal catalysis enables some of the most synthetically powerful reactions. While the general focus is often given to the metal center, careful crafting of the microenvironment surrounding the center, through well-fitting ligand architectures, is fundamental to achieve the targeted activity and selectivity. In analogy to a protein scaffold in metalloenzymes — nature's metal catalysts — the ligand creates the active site around the metal and controls the catalytic process.



3D model of xantphos coordinating to a metal.

Xantphos (pictured) — a formal merger of two simple triphenylphosphine motifs into a single ligand built on a xanthene scaffold — represents one of the success stories of ligand development. Specifically, it forms complexes with a wide range of metals, which in turn are used in a broad spectrum of catalytic methods, including hydroformylations, hydrocyanations, carbonylations, cross-couplings, C–H activation reactions forming C–C and C–X bonds. But what exactly makes xantphos so versatile?

Xantphos contains two phosphine moieties that can strongly bind to a metal center in a bidentate fashion, leading to the formation of a well-defined complex. Both phosphine sites are set well apart across the xanthene scaffold resulting in a wide “bite angle” of 111° (the ligand–metal–ligand bond angle, pictured)<sup>3</sup>, in contrast to typical bidentate ligands that offer smaller bite angles of around 90°. The geometry of xantphos inherently favours the formation

of trigonal or tetrahedral complexes, while 90° bite angle ligands favour the formation of square-planar complexes. This means that xantphos can readily form catalytic intermediates that are often most relevant in chemical processes, which would be more difficult to accommodate with other ligands.

In fact, such geometrical considerations were at the origin of the initial design of xantphos by van Leeuwen in 1995 during his studies on the hydroformylation of alkenes (one of the most important catalytic processes in industry with over 10-million-ton annual production). The xantphos-based Rh-catalyst turned out to be — and remains — among the most active and selective catalysts developed<sup>4</sup>. Xantphos was later exploited in the discovery of a range of new transformations as well as in the advancement of a number of established processes<sup>5</sup>. The broad scaffold of xantphos also supports its simultaneous coordination to two metal centers, thereby stabilizing unusual binuclear complexes. This feature is instrumental for Pd-catalyzed hydroformylation reactions offering unusual selectivities<sup>6</sup>.

Over the years, multiple other features of xantphos have been uncovered. For instance, although it is typically considered to be bidentate with a fixed wide bite angle, this seems to not always be the case in a catalytic process. The xanthene scaffold is somewhat flexible, meaning xantphos can adapt to a wide range of potential bite angles. Further, the central oxygen site might also partake in metal–ligand coordination. In consequence, xantphos can readily shift between different bite angles and mono-, bi-, and tridentate binding modes during a catalytic process, stabilizing each consecutive catalytic intermediate as temporarily required. In addition, the hemilabile character of xantphos imposed by the central oxygen — the ability of one site to coordinate and dissociate readily from the metal center<sup>7</sup> — can also assist the exchange processes occurring at the metal center, thereby facilitating the catalytic activities.

Besides, although the oxidation of phosphine ligands is typically detrimental for their function in a catalytic process, the partial oxidation of the ligand has been shown to be key in xantphos–Pd-catalyzed C–H activation reactions<sup>8</sup>. Specifically, during the initial activation of the pre-catalyst, one of the phosphine motifs undergoes oxidation. The resulting bisphosphine mono-oxide then acts as a functional hemilabile ligand in the catalytic process, which has been shown to be more efficient than its non-oxidized counterpart.

Overall, given its capacity, xantphos belongs to a class of versatile ligands, along with others such as triphos (tridentate phosphine), IPr (*N*-heterocyclic carbene), bpy (2,2'-bipyridine), or Cp\* ( $\kappa^5\text{-C}_5\text{Me}_5^-$ ) that have been shown to enable catalytic activity of transition metal complexes in various processes. Arguably, they should be considered as “privileged ligands” in analogy to “privileged chiral ligands” that enable stereoselectivities in various asymmetric processes<sup>9</sup>. As the development of new ligands enabling specific reactivities remains of central importance in catalysis, the versatility of xantphos shows that a seemingly simple ligand can go a long way.

## References

1. Catlow, C. R., Davidson, M., Hardacre, C. & Hutchings, G. J. *Phil. Trans. R. Soc. A.* **374**, 20150089 (2016).
2. Thayer, A. M. *C&EN* **91**, 64–68 (2013).
3. Casey, C. P. & Whiteker, G. T. *Isr. J. Chem.* **30**, 299–304 (1990).
4. Kranenburg, M. *et al.* *Organometallics* **14**, 3081–3089 (1995).
5. van Leeuwen, P. W. N. M. & Kamer, P. C. J. *Catal. Sci. Technol.* **8**, 26–113 (2018).
6. Zhang, Y., Torker, S., Sigrist, M., Bregović, N. & Dydio, P. *J. Am. Chem. Soc.* **142**, 18251–18265 (2020).
7. Adams, G. M. & Weller, A. S. *Coordination Chemistry Reviews* **355**, 150–172 (2018).
8. Ji, Y. *et al.* *J. Am. Chem. Soc.* **137**, 13272–13281 (2015).
9. Yoon, T. P. & Jacobsen, E. N. *Science* **299**, 1691–1693 (2003).