Coordination Chemistry Reviews 255 (2011) 2860–2881

Contents lists available at ScienceDirect

Coordination Chemistry Reviews

journal homepage: www.elsevier.com/locate/ccr

Review

Synthesis and coordination chemistry of macrocyclic phosphine ligands

Charles D. Swor, David R. Tyler*

Department of Chemistry, University of Oregon, Eugene, OR 97403, United States

Contents

ARTICLE INFO

Article history:
Received 21 March 2011
Accepted 7 June 2011
Available online 2 July 2011

Keywords:
Phosphines
Macrocyclic ligands
Ligand synthesis
Template synthesis
Reactions of coordinated ligands

ABSTRACT

Macrocyclic phosphine compounds are sought after as ligands for transition metal complexes because of their strong binding properties. As such, these ligands are particularly useful in applications where robust transition metal–phosphine complexes are employed, as in homogeneous catalysis or in radiopharmaceuticals. This review summarizes the development of macrocyclic phosphine ligands, including their preparation and coordination to transition metals. Synthetic methods for the preparation of phosphine macrocycles are discussed, including methods for controlling ring size and stereochemistry. The coordination chemistry of macrocyclic phosphines is also reviewed. Many phosphine macrocycles are synthesized by template methods, and methods for removing the templating metal from the macrocyclic ligand are reviewed.

1. Introduction

Phosphines (PR_3) are an important class of compound because of their widespread use as ligands for transition–metal complexes. Phosphine ligands are soft, strong σ-donors, and their electronic, steric, and stereochemical properties vary based on the substituents attached to the phosphorus atoms [1–3]. Thus, choosing the correct phosphine ligands for a metal complex allows control over the electronic and steric environment of the complex [4]. Such tunability is most useful for optimizing the activity of homogeneous catalysts, and as such a plethora of phosphine-containing homogeneous catalysts have been developed for a wide variety of organic reactions including hydrogenation, hydroformylation, hydration, hydrolysis, cross-couplings, and carbon-heteroatom

* Corresponding author. Tel.: +1 541 346 4649; fax: +1 541 346 0487.
E-mail address: dtyler@uoregon.edu (D.R. Tyler).

0010-8545/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.ccr.2011.06.002

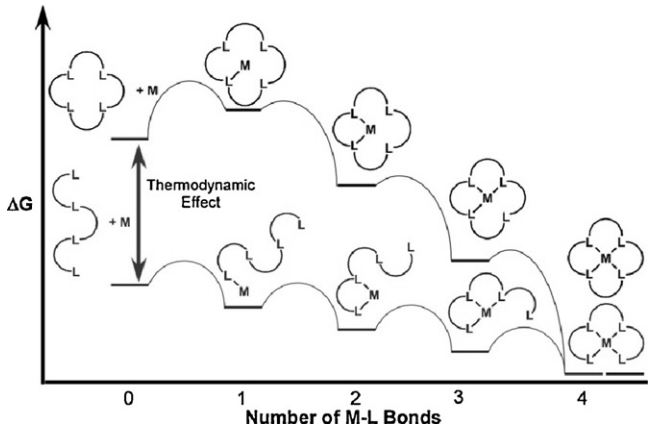

Fig. 1. Origin of the thermodynamic macrocyclic effect.

bond formations [5]. In addition, transition–metal phosphine complexes activate small molecules such as H_2, O_2, N_2, H_2O, and CO_2 [6], which makes them promising candidates for use in hydrogen fuel cells, water-splitting, ambient-pressure ammonia synthesis, and artificial photosynthesis.

Macrocyclic ligands – ligands that form a large, continuous ring around a metal ion – form extremely robust complexes because of the *macrocyclic effect* [7]. This effect has both thermodynamic and kinetic origins. The *thermodynamic macrocyclic effect* refers to the higher binding constant ($\log \beta$) for a macrocyclic ligand compared to an analogous open-chain ligand (Eq. (1)):

$$\text{Macrocyclic effect} = \Delta \log \beta = \log \beta_{\text{macrocycle}} - \log \beta_{\text{open-chain}} \quad (1)$$

Because the macrocyclic ring lacks a "free end," stepwise removal of the donor atoms is exceedingly difficult. This feature results in very slow dissociation rates of macrocyclic ligands from their complexes (the *kinetic macrocyclic effect*).

The energetic basis for the macrocyclic effect can be most easily understood by comparing the relative stabilities of *unbound* macrocyclic ligands to open-chain ligands as illustrated in Figs. 1 and 2 [8–10]. (Note in these figures that the *coordinated* macrocyclic and open-chain complexes have been arbitrarily set at equal energies.) As indicated in the figures, a free macrocyclic ligand in solution is less stable than its open-chain analog because of reduced flexibility and the resulting loss of configurational entropy. Macrocycles also have less solvent-accessible surface area and cannot be as efficiently stabilized by interactions with solvent molecules. This solvent interaction is especially important for nitrogen macrocycles in aqueous solution, where the free open-chain ligand can extend and the nitrogen atoms can accept hydrogen bonds from the solvent. By contrast, macrocyclic nitrogen ligands are conformationally restricted, and the nitrogen atoms are not as accessible for hydrogen bonding, resulting in poor stabilization of the free macrocycle. Because of this, the macrocyclic effect in nitrogen ligands is especially large (up to $\log \beta \sim 10$) [11]. Macrocyclic oxygen ligands (crown ethers), which bind electrostatically to alkali metals and other cations, show smaller macrocyclic effects ($\log \beta \sim 3$–4) [12], which are primarily attributed to enthalpic contributions [13]. Macrocyclic sulfur ligands show an even smaller macrocyclic effect ($\log \beta \sim 2$) [14], although it has been shown that additional functionalization (installation of *gem*-dimethyl groups) can help to further stabilize macrocyclic sulfur complexes [15].

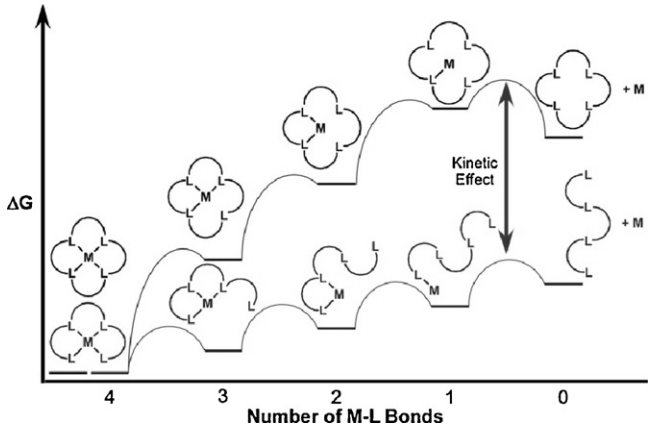

Fig. 2. Origin of the kinetic macrocyclic effect.

Macrocyclic phosphines hold promise as incredibly stable ligands for applications requiring robust complexes, such as radioactive transition metal complexes for use as radiopharmaceuticals [16,17]. Because of this possibility, these ligands and their complexes have been synthetic targets since soon after the macrocyclic effect was discovered. Unfortunately, macrocyclic phosphine ligands have historically been difficult to synthesize in good yield. A general, versatile synthesis of phosphine macrocycles has not yet been developed, for reasons that will be discussed below. Also, the macrocyclic effect has not yet been measured for a phosphine ligand. This is due to the difficulty in synthesizing macrocyclic ligands, as well as open-chain reference ligands, as will be discussed further below.

The focus of this review is on advances in both the synthesis and coordination chemistry of macrocyclic phosphine ligands. Several reviews of phosphorus-containing macrocycles have been published [18–21], but none have focused specifically on macrocyclic phosphine ligands. Generally, the term *macrocycle* is used when describing a ring of at least nine covalently bonded atoms, which is not part of a system of fused or bridged smaller rings. This review, then, will only consider macrocycles with at least nine-membered rings. Also, because macrocyclic ligands are generally considered to be polydentate, this review will only cover macrocycles with at least three phosphorus donor atoms as part of the ring. Mixed-donor macrocycles will not be thoroughly reviewed, but will be mentioned in instances when they accompany similar all-phosphorus-donor macrocycles. Finally, this review will also include macrocycles containing functional groups that can be routinely converted to phosphines. For example, phosphine oxides and phosphine sulfides can be converted to phosphines by reduction with $LiAlH_4$ or silanes, and quaternary phenylphosphonium or benzylphosphonium ions can be converted by either reductive cleavage with $LiAlH_4$ or by base hydrolysis to the phosphine oxide, followed by reduction. Because these conversions are possible, the synthesis of macrocycles containing these functional groups can be thought of as *formal* syntheses of phosphine macrocycles; as such, these cases are included in this review.

2. Synthesis of macrocyclic phosphine ligands

2.1. Cyclocondensation reactions

2.1.1. Early syntheses

The first macrocyclic phosphine ligands were synthesized in 1975 by Horner et al. [22,23]. These phosphines were generated by the tetramolecular "2:2" reaction of 2 equivalents of α,ω-bis(dibenzyl)phosphines with 2 equivalents of α,ω-dialkyl halides to form 16-, 18-, and 20-membered macrocyclic quaternary benzylphosphonium salts **1** (Scheme 1, Method A). The yields of the phosphonium macrocycles generated by this method were very low (3–11%). In most cases, the bimolecular "1:1" small-ring