Pergamon

Tetrahedron: *Asymmetry* 14 (2003) 3427–3429

TETRAHEDRON:
ASYMMETRY

Assignment of the structure of a Ru(II)–BINAP catalyst☆

Lisa DiMichele,* Steven A. King† and Alan W. Douglas‡

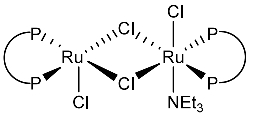
Department of Process Research, Merck Research Laboratories, Rahway, NJ 07065, USA

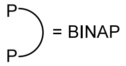
Received 23 June 2003; accepted 5 August 2003

Abstract—Ruthenium–BINAP catalysts are commonly used in asymmetric hydrogenations and provides high enantioselectivity over a wide range of substrates. Herein we focus on a single Ru(II)–BINAP catalyst prepared from cyclooctadienyl ruthenium dichloride and (*R*)-BINAP in the presence of triethylamine and report on the structure identified using NMR as the diethylammonium salt $[(C_2H_5)_2NH_2]^+[Ru_2Cl_5((R)\text{-BINAP})_2]^-$.

1. Introduction

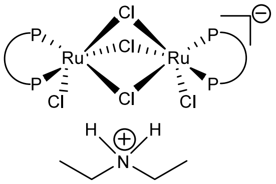
In 1985 a Ru(II)–BINAP catalyst, which provided an extremely high yield and high enantioselectivity in the reduction of β-ketoesters, was reported.[2] It was synthesized from $[Ru(COD)Cl_2]_n$, BINAP, and triethylamine, and its structure postulated to be the triethylamine solvate **1**.[3] Since then a broad range of hydrogenation substrates have been reported.[4]





1

Other catalysts and catalyst preparations have also been described,[5–9] however, the triethylamine solvate **1** and its related systems have been used extensively for the syntheses of pharmaceutical intermediates.[1,9–11] During our research on the mechanism action of this catalyst, we noted certain inconsistencies between the spectroscopic properties of the material and its postulated structure, **1**.[3] Herein we report that the compound is in fact the diethylammonium salt $[Et_2NH_2]^+$ $[Ru_2Cl_5(BINAP)_2]^-$, **2**.[§]



2

2. Results and discussion

In our original work on the synthesis of the Ru(II)–BINAP catalyst, we assumed the structure to be **1**.[9] This was based on NMR data collected at ambient temperature as well as literature precedent.[2] However, upon re-examination of the ^{31}P data as well as further NMR studies (discussed below) on the catalyst at low temperature, the structure was shown to be **2.** Catalyst **2** has the advantage of being readily prepared in a highly pure form. The reaction of $[RuCl_2(COD)]_n$, triethylamine, and BINAP in toluene at reflux provides a brick red solution from which the product crystallizes as a toluene solvate upon cooling. After drying, a microcrystalline powder (mp 210°C dec.) is obtained which is birefringent, but gives only a weak X-ray

---

[☆] Portions of this work were reported at the Organic Reactions Catalysis Society meeting, May 4–8, 1994; Phoenix, Arizona. King, S. A.; DiMichele, L. *Chem. Ind.* (“*Catalysis of Organic Reactions*”) **1995**, *62*, 157.[2]

[*] Corresponding author. E-mail: lisa_dimichele@merck.com; steve.king@abbot.com

[†] Present address: Department of Process Research and Development, Abbott Laboratories, Chicago, IL 60064, USA.

[‡] Retired.

[§] ^1H NMR (CD_2Cl_2, 400.13 MHz) δ 8.53 (br s, 2H), 8.07 (t, $J=8.8$ Hz, 4H), 7.82 (t, $J=8.3$ Hz, 2H), 7.65 (om, 6H), 7.55 (m. 4H), 7.47 (m, 4H), 7.39–7.12 (om, 18H), 6.95 (m, 2H), 6.84 (t, $J=7.4$ Hz, 2H), 6.78–6.72 (om, 4H), 6.70–6.63 (om, 4H), 6.59–6.50 (om, 12H), 3.24 (om, 4H), 1.45 (t, $J=7.3$ Hz, 6H).

0957-4166/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2003.08.037

powder diffraction pattern. We have not yet been able to grow a single crystal suitable for X-ray analysis. Also the material only shows useful solubility suitable for NMR study in chlorinated solvents.

Upon re-examination of the ^{31}P data in combination with low temperature ^{1}H studies, we concluded that structure **1** was inconsistent with the NMR data. The proton decoupled ^{31}P NMR spectrum of the catalyst matches the data provided in the original report.[2] The simple AB quartet results from two diastereotopic phosphorus atoms coupled to one another. This spectrum indicates high symmetry in the complex assuming no exchange processes are occuring.[12]

In the ^{1}H NMR spectrum, integration of the ethylamino protons (δ 1.41 and 3.23) against the aromatic region gives values which are two-thirds of that expected for structure **1** despite the use of extended relaxation delays. When the purified catalyst is prepared by our previously published procedure[9] and cooled to −40°C in methylene chloride-d_2 solution, the enantiotopic methylene protons of the ethylamino groups become baseline resolved. As shown in the bottom trace in Figure 1, the coupling pattern for these protons is more complex than that expected for a triethylamine molecule. We also observed an apparently extraneous broad peak integrating for two protons at δ 8.51. When this resonance was decoupled, the ethylamino protons simplified to a doublet of quartets (J=13.1, 7.5 Hz). A doublet of triplets (J=13.1, 5.0 Hz) resulted when the attached methyl group was irradiated. This coupling pattern is only consistent with a diethylammonium cation. In fact, spiking experiments showed that the ethylamino resonances coalesce with added diethylamine, but not triethylamine.

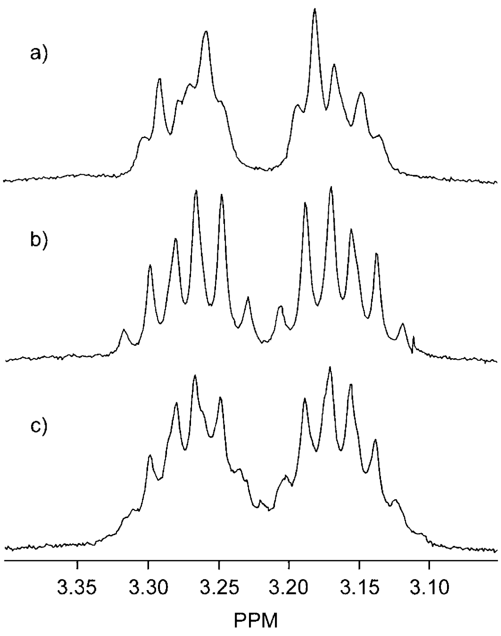


Figure 1. Diastereotopic methylene protons of diethylammonium cation at −40°C: (a) with decoupling at δ 1.41; (b) with decoupling at δ 8.53; (c) fully coupled.

We inferred that the baseline resolution of the methylene protons must be as a result of tight ion-pairing with a Ru–BINAP containing anion in methylene chloride solution. Structure **2**, which results from the addition of a third bridging chloride to structure **1**, seemed a good candidate. This assignment has the advantage of putting both ruthenium atoms in an octahedral environment while maintaining bridging halide ligation. Combustion analysis data were in excellent agreement with this suggestion (calculated: C, 66.39; H, 4.73; N, 0.78; P, 6.92; Cl, 9.90; found: C, 66.06; H, 4.74; N, 0.74; P, 6.91; Cl, 9.79).[13] The chlorine analysis was most important in identifying the anionic dimer as the correct structure since it defined the stoichiometry of the complex as five chlorines to four phosphorus atoms. Positive ion electrospray mass spectroscopy also confirmed the molecular formula (Fig. 2).

Strong literature precedent for structure **2** is found in the publications of the James group, who prepared analogous anionic dimers with the chelating phosphines dppb, dppp, diop, and chiraphos by a different route.[14] The crystal structure of the dppb compound has also been reported.[15]

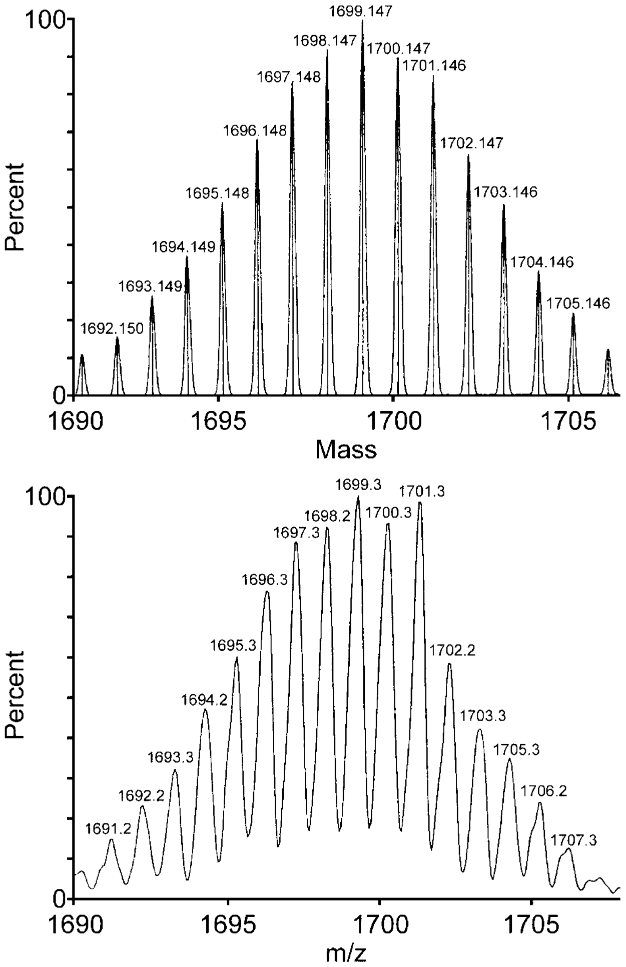


Figure 2. Positive ion electrospray mass spectrum calculated (top) versus actual (bottom).

The triethylamine used in our studies were shown to be free of diethylamine. The presence of diethylamine in the reaction mixture can only be accounted for by decomposition of triethylamine. Since the reaction mixture contains both a base and a good Lewis acid [Ru(II)], elimination of ethylene at the high reaction temperature is a mechanistic possibility. Dealkylation of tertiary amines in the presence of Ru(II) complexes has also been observed by James et al.[16]

The most important implication of the new assignment is that the saturated octahedral environment of **2** would be expected to be unreactive. Thus, **2** should be a poor catalyst. Indeed, we have found that activation with acid is necessary to obtain low pressure (40 psi) and low temperature (40°C) catalytic hydrogenation reactions.[9,17,18]

Acknowledgements

We thank Professor Bruce Lipshutz's group at the University of California-Santa Barbara for acquiring the electrospray mass spectral data.

References

1. Douglas, A. W., DiMichele, L., King, S. A., Verhoeven, T. R.; U. S. Patent No. 5,596,113, Jan. 21, 1997
2. Ikariya, T.; Ishii, Y.; Kawano, H.; Arai, T.; Saburi, M.; Yoshikawa, S.; Akutagawa, S. *J. Chem. Soc., Chem. Commun.* **1985**, 922.
3. Kawano, H.; Ikariya, T.; Ishii, Y.; Saburi, M.; Yoshikawa, S.; Uchida, Y.; Kumobayashi, H. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1571.
4. For a review, see: Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345.
5. Mashima, K.; Kusano, K.; Ohta, T.; Noyori, R.; Takaya, H. *J. Chem. Soc., Chem. Commun.* **1989**, 1208.
6. Mashima, K.; Kusano, K.; Sato, N.; Matsumura, Y.; Nozaki, K.; Kumobayashi, H.; Sayo, N.; Hori, Y.; Ishizaki, T.; Akutagawa, S.; Takaya, H. *J. Org. Chem.* **1994**, *59*, 3064.
7. Kitamura, M.; Tokunaga, M.; Ohkuma, T.; Noyori, R. *Tetrahedron Lett.* **1991**, *32*, 4163.
8. Kitamura, M.; Tokunaga, M.; Ohkuma, T.; Noyori, R. *Org. Synth.* **1992**, 71.
9. King, S. A.; Thompson, A. S.; King, A. O.; Verhoeven, T. R. *J. Org. Chem.* **1992**, *57*, 6689.
10. Noyori, R. *Chem. Tech.* **1992**, *6*, 360.
11. Armstrong, J.; King, S. *Org. Synth.*, in press.
12. The spectrum is invariant to −100°C.
13. Calculated for structure **1**: C, 66.79; H, 4.71; N, 0.83; P, 7.33; Cl, 8.39
14. James, B. R.; Pacheco, A.; Rettig, S. J.; Thorburn, I. S.; Ball, R. G.; Ibers, J. A. *J. Mol. Catal.* **1987**, *41*, 147.
15. Gamage, S. N.; Morris, R. H.; Rettig, S. J.; Thackray, D. C.; Thorburn, I. S.; James, B. R. *J. Chem. Soc., Chem. Commun.* **1987**, 894.
16. Joshi, A. M.; Thorburn, I. S.; Rettig, S. J.; James, B. R. *Inorg. Chim. Acta* **1992**, *198-200*, 283.
17. Douglas, A. W.; Abramson, I. N.; Houpis, I. N.; Karady, S.; Molina, A.; Xavier, L. C.; Yasuda, N. *Tetrahedron Lett.* **1994**, *35*, 6807.
18. In unreported work we have accomplished catalyst activation with a variety of Lewis acids, in addition to protic acid reported in Refs. 1 and 6.