

The Synthesis of Glycosyl Phosphite-Pt(II) Complexes

Ling Hua CAO^{1,2}*, Hong Yun GAO^{1,2}, Chuan Jian ZHOU^{1,2}, Yu Ting LIU¹

¹ College of Chemistry and Chemical Engineering, Xinjiang University, Urumqi 830046

² State Key Laboratory of Elements-Organic Chemistry, Nankai University, Tianjin 300071

Abstract: Ethylene glycol phosphorochloridite **1** or catechol phosphorochloridite **2** reacted with isopropylidene derivatives of D-glucose, D-galactose, D-mannose and D-fructose, a series of glycosyl phosphites were obtained. These glycosyl phosphites form optically active complexes with simple Pt (II) salts. Pt (II) is coordinated to the phosphorus atom, most of the metal complexes are quite stable.

Keywords: Glycosyl phosphite, metal complex, synthesis.

Sugar derivatives whose molecules contain trivalent phosphorus groups have been coming into use for different scientific purposes, including the synthesis of metal complexes. These metal complexes of glycosyl phosphites are effective chiral catalysts in enantioselective synthesis¹⁻⁵ such as hydrogenation, cyclopropylation, hydrophosphination and hydrosilylation of achiral olefin. Furthermore, this kind of compounds are also widely applied in biology and medicine area and open up a new field of research⁶⁻⁸. They can adjust the growth of organism cell and their *cis*-platinum complexes possess anticancer and antitumor activities.

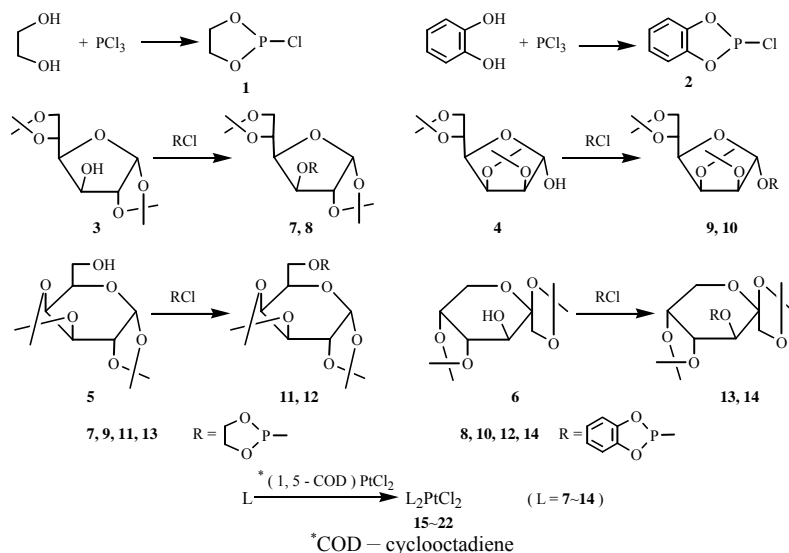
This article reports a new type of carbohydrate ligand, framework glycosyl mono-phosphite (1,2:5,6-di-*O*-isopropylidene- α -D-glucofuranose)-ethylene glycol phosphite **7**, (1,2:5,6-di-*O*-isopropylidene- α -D-glucofuranose)-catechol phosphite **8**, (2,3:5,6-di-*O*-isopropylidene- α -D-mannopyranose)-ethylene glycol phosphite **9**, (2,3:5,6-di-*O*-isopropylidene- α -D-mannopyranose)-catechol phosphite **10**, (1,2:3,4-di-*O*-isopropylidene- α -D-galactopyranose)-ethylene glycol phosphite **11**, (1,2:3,4-di-*O*-isopropylidene- α -D-galactopyranose)-catechol phosphite **12**, (1,2:4,5-di-*O*-isopropylidene- β -D-fructopyranose)-ethylene glycol phosphite **13**, (1,2:4,5-di-*O*-isopropylidene- β -D-fructopyranose)-catechol phosphite **14**, and a series of Pt (II) metal complexes with new ligand have been reported. All the process is shown in **Scheme 1**.

To trivalent phosphorus, ³¹P NMR can not only monitor the process of reactions but also can determine the structure of these compounds.

Reaction of 1,2:5,6-di-*O*-isopropylidene- α -D-glucofuranose **3**, 2,3:5,6-di-*O*-isopropylidene- α -D-mannofuranose **4**, 1,2:3,4-di-*O*-isopropylidene- α -D-galactopyranose **5**, or 1, 2:4, 5-di-*O*-isopropylidene- β -D-fructopyranose **6** with ethylene glycol phosphoro-

* E-mail: clhxj@xju.edu.cn

Scheme 1



chloridite **1** or catechol phosphorochloridite **2** under mild condition yielded the glycosyl phosphite **7-14**. These products reveal a signal at δ_{p} 130 to 140 in ^{31}P NMR, confirming that the reactions between the phosphorochloridites and sugar derivatives occurred.

The platinum cyclooctadienyldichlorides coordinated with phosphite **7-14** readily and completely under mild conditions, gave *cis*-platinum complexes. The structures were supported by ^{31}P NMR and elemental analysis. Along with the singlets, ^{31}P NMR spectra of all platinum adducts exhibited two satellite peaks. It was caused by the magnetic interaction between nuclei ^{31}P and ^{195}Pt . According to NMR data, similar *cis*-complexes formed at a ratio $\text{P} : \text{Pt} \text{ ca. } 2 : 1$. The coupling constants were more than 5500 Hz and δ_{p} was 82~95. But when (2, 3:5, 6-di-*O*-isopropylidene- α -D-Mannofuranos-1-yl)-phosphite acted as ligand, the coupling constants were below 4000 Hz, it is because phosphorus atom linked with hydroxy group of C-1.

Ethylene glycol phosphorochloridite **1** was obtained from equimolar ethylene glycol and PCl_3 in chloroform or ether. After evaporating the solvent under reduced pressure, the product was distilled *in vacuo*, bp 66~68 °C/47 mmHg, d^{20} 1.4196, δ_{p} 167, yield 72%.

Catechol phosphorochloridite **2** was obtained from 0.1 mol catechol and 0.5 mol PCl_3 . The product was distilled *in vacuo*. Yield was 80%, bp 70~71 °C /7 mmHg, mp 30°C, δ_{p} 167.

The compounds **7-14** were obtained from compounds **3-6**, phosphorochloridites (**1** or **2**) and Et_3N in benzene. The reaction mixture was intensively stirred at room temperature and tested by TLC to completion. The precipitate formed was filtered off and the benzene solution was concentrated under reduced pressure to a thick syrup, which was purified by column chromatography. The analytical data were shown in

Table 1 The physical data of compounds 7~14

No.	Yield %	Outward	Elemental analysis Found (Calcd.)		
			C	H	P
7	45.4	Light yellow syrup	48.10 (48.00)	6.54 (6.62)	8.87 (8.84)
8	46.2	Light yellow syrup	54.36 (54.27)	5.75 (5.82)	7.82 (7.78)
9	39.2	Colorless syrup	48.04 (48.00)	6.57 (6.62)	8.85 (8.84)
10	50.3	Colorless syrup	54.38 (54.27)	5.76 (5.82)	7.81 (7.78)
11	41.3	Light yellow syrup	48.15 (48.00)	6.56 (6.62)	8.87 (8.84)
12	48.5	Light yellow syrup	54.41 (54.27)	5.79 (5.82)	7.83 (7.78)
13	40.1	Colorless syrup	47.91 (48.00)	6.68 (6.62)	8.88 (8.84)
14	39.2	Colorless syrup	54.39 (54.27)	5.78 (5.82)	7.73 (7.78)

Table 2 ¹H NMR and ³¹P NMR chemical shift of compounds 7~14

No.	¹ H NMR δ ppm (CDCl ₃)						³¹ P NMR δ ppm
	H-1	Glycosyl-ring H-2,3,4,5	H-6	C-CH ₃	OCH ₂	Phenyl-H	
7	5.84 (d)	4.04~4.55	3.95	1.46~1.67	3.67		139
8	5.80 (d)	3.99~4.56	3.59	1.46~1.68		7.08	138
9	5.62 (m, ³ J _{P-H} 7.61)	3.95~4.78	3.88	1.50~1.76	3.65		131
10	5.64 (m, ³ J _{P-H} 7.65)	3.96~4.79	3.89	1.51~1.77		7.10	133
11	5.52 (d)	4.08~4.68	3.86	1.33~1.70	3.69		137
12	5.50 (d)	4.09~4.66	3.81	1.31~1.69		7.03	138
13	H-2 3.94 (d)	H-3,4,5 4.05~4.31	3.83	1.35~1.54	3.66		139
14	3.93 (d)	4.00~4.32	3.82	1.36~1.56		7.13	138

Table 3 The data of elemental analysis of compounds 15~22

Compd.	Elemental analysis Found (Calcd.)				
	C	H	Cl	P	Pt
15	34.68 (34.79)	4.87 (4.80)	7.23 (7.34)	6.49 (6.41)	20.32 (20.18)
16	40.87 (40.69)	4.29 (4.36)	6.78 (6.67)	5.78 (5.83)	18.48 (18.36)
17	34.87 (34.79)	4.72 (4.80)	7.41 (7.34)	6.51 (6.41)	20.10 (20.18)
18	40.77 (40.69)	4.25 (4.36)	6.79 (6.67)	5.76 (5.83)	18.30 (18.36)
19	34.83 (34.79)	4.77 (4.80)	7.48 (7.34)	6.36 (6.41)	20.01 (20.18)
20	40.79 (40.69)	4.33 (4.36)	6.72 (6.67)	5.75 (5.83)	18.29 (18.36)
21	34.97 (34.79)	4.69 (4.80)	7.29 (7.34)	6.46 (6.41)	20.31 (20.18)
22	40.76 (40.69)	4.31 (4.36)	6.76 (6.67)	5.79 (5.83)	18.28 (18.36)

Table 4 The physical data of compounds 15~22

Compd.	Yield %	mp °C	³¹ P NMR		MS (ESI) M ⁺ m/z
			δ	J _{PLP}	
15	53.4	105~107	183, 93, 5	5742.2	1221, 1223
16	56.6	129~131	174, 84, -5	5763.8	1317, 1319
17	60.3	98~100	186, 89, 2	3941.3	1221, 1223
18	62.9	112~114	181, 95, 9	3836.1	1317, 1319
19	54.7	96~97	178, 89, 1	5694.6	1221, 1223
20	55.1	107~109	171, 84, -4	5615.7	1317, 1319
21	62.1	113~115	176, 88, 0.2	5713.5	1221, 1223
22	64.7	121~123	173, 84, -5	5738.0	1317, 1319

Table 1, ¹H NMR and ³¹P NMR data were shown in **Table 2**.

The compounds 15~22 were obtained from phosphite 7~14 (2 mmol) and

(1,5-COD)PtCl₂ (1 mmol) in dichloromethane solution. The mixture was stirred for 1 h at room temperature and 15 mL of hexane was added. The precipitate was filtrated off and recrystallized from CH₂Cl₂-Me₂CO 1 : 1. The physical data of compounds **15~22** were shown in **Table 3** and **Table 4**.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (Grant No. 29962002) and Nankai University State Key Laboratory of Elemento-Organic Chemistry.

References

1. G. J. Buisman, M. E. Martin, J. J. Vos, A. A. Klootwijk, *Tetrahedron: Assymtry*, **1995**, *6*, 719.
2. A. Harthun, R. Kadyrau, R. Selkl, R. Barga, *Angew. Chem. Int. Ed. Eng.*, **1997**, *36*, 1107.
3. H. J. Reetz, W. Vogel, *ibid.*, **1997**, *36*, 865.
4. T. V. Rajanbabu, T. A. Ager, G. A. Holliday, *J. Org. Chem.*, **1991**, *62* (17), 6012.
5. P. Barbaro, A. Currao, J. Hermann, *Organometallics*, **1996**, *15* (7), 1879.
6. H. Sigel (Ed), *Metal Ions in Biological System*, Dekker, New York, **1980**, Vol. *12*.
7. M. J. Cleare, P. L. Hydes, *Tetrahedron: Assymtry*, **1995**, *11*, 1.
8. J. S. Thompson, R. L. Harlow, J. F. Whitney, *J. Am. Chem. Soc.*, **1983**, *105* (11), 3522.
9. E. E. Nifantsev, M. P. Koroteev, M. K. Aleksander, V. K. Belsky, A. I. Stash, M. Yu. Antipin, K. A. Lysenko, L. H. Cao, *J. Organometallic Chem.*, **1999**, *587*, 18.

Received 12 Feruary, 2003