Pergamon

Tetrahedron Letters, Vol. 35, No. 38, pp. 7019-7022, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)01527-9

A Versatile Key Synthon for the Syntheses of Ligands Potentially Suited for the Preparation of μ-Phenoxo Dimetallic Complexes with Two Non Equivalent Complexation Sites

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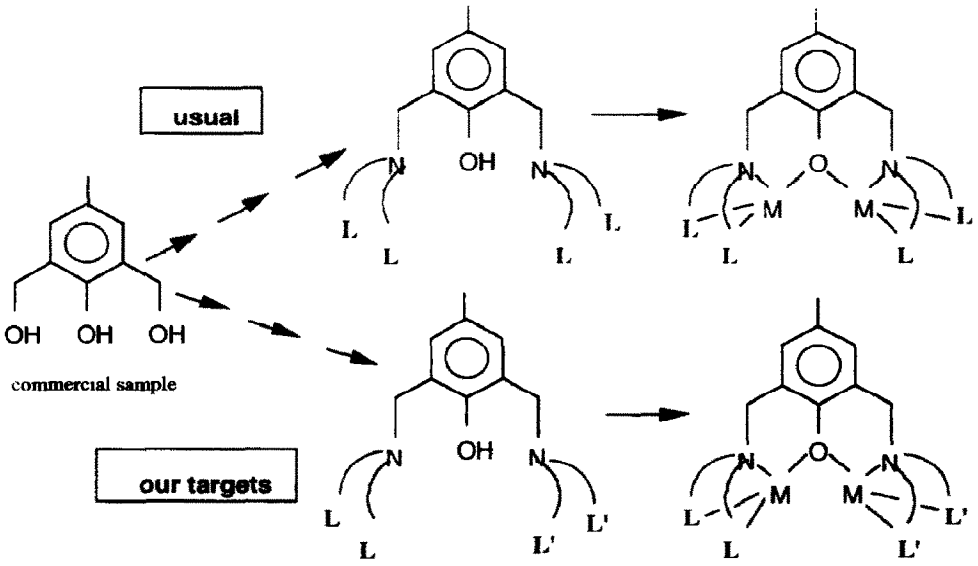
Abstract : The synthon S, easily prepared in two steps (65% yield) from 2,6 - bis (hydroxymethyl)- 4 -methylphenol, may allow the syntheses of various dinucleating ligands bearing two chemically different coordination environments . The preparation of the dinucleating ligands from S implies three steps .

Transition metal complexes of polypodal binucleating ligand systems provide the opportunity to study the magnetic exchange interaction and the multi-electron redox processes between the two metal centers and the activation of small molecules such as N_2 or O_2. They have received much attention as models of several metalloproteins.[1-6] Almost all of the complexes described in literature imply equivalent environments of the two metal ions, since the use of symmetrical polypodal dinucleating ligands greatly simplify the synthetic problem .

We describe herein a simple synthetic strategy, allowing the obtention of ligands potentially suited for the preparation of dimetallic complexes implying two non equivalent complexation sites . Because simple oxo-bridged complexes are known to dissociate, we have focused our attention on phenoxo-bridging dinucleating ligand systems [Scheme 1] .

Our synthetic strategy is depicted in Scheme 2 ; it implies the key synthon S, which is prepared in two steps from a commercial sample of 2, 6 - bis (hydroxymethyl) - 4 - methyl phenol, with a 65% yield.[7] It must be emphasized that usual binucleating ligands (L = L') may also be prepared from the synthon S, by using the same L-CH_2-NH-CH_2-L reagent in the steps (iii) and (v) .



L, L' : mono or bidentate ligands for transition metal ions
M : $Fe^{II,III}$; $Mn^{II,III,IV}$; $Cu^{I,II}$; Co^{II} .....

The coordination sphere of each metal ion may be achieved by exogenous bridging ligands (e .g . acetate) or by monodentate ligands such as chloride, water, solvent...

Scheme 1

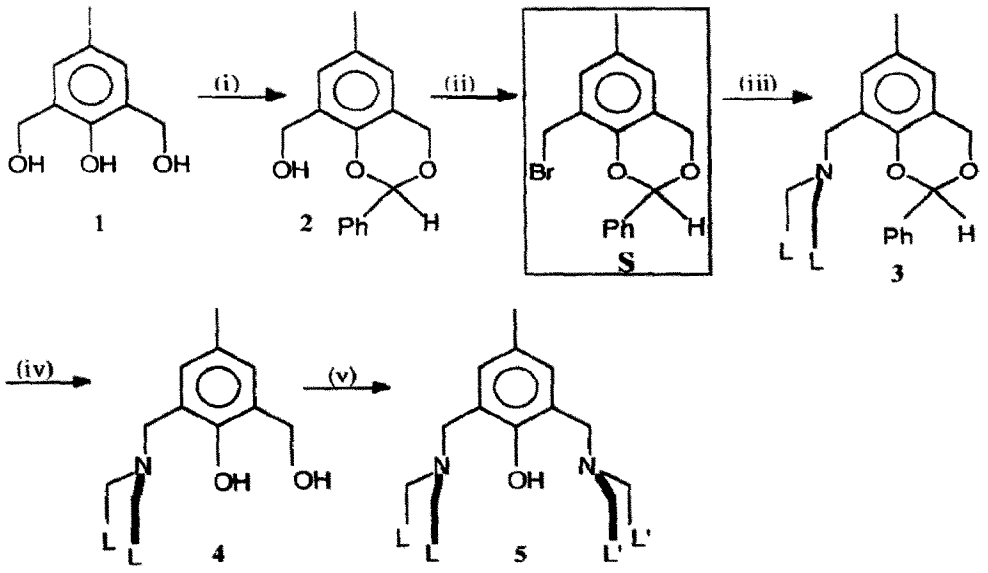
General procedure

Synthon S :

(i) : A mixture of 2,6-bis-(hydroxymethyl)-4-methylphenol (20g, 119 mmol), benzaldehyde dimethylacetal (22.3 g, 146 mmol) and p.toluene sulfonic acid monohydrate (400 mg) in DMF (100ml) was rotated under aspirator pressure at 50°C for 5.5 hours ; the crude product (t.l.c. on silicagel, pentane/ethyl acetate 5/2, Rf = 0.47) was diluted with chloroform and washed successively with a solution of sodium hydrogen carbonate, water saturated with NaCl and dried (Na_2SO_4). After filtration and removal of solvent, the crude compound solidified with time and was recrystallized from hexane / ethyl acetate 8/1 (white crystal ; m.p 95° C ; yield : 85 %). Spectroscopic data (^1H and ^{13}C NMR, IR and MS) are consistent with the assigned structure .

(ii) : To a solution of this product (10g, 39 mmol) in 200 ml of anhydrous DMF, were added under nitrogen atmosphere 19.4 g (58 mmol) of carbon tetrabromide . The resulting solution was cooled in an ice bath and 15.35 g (58 mmol) of triphenyl phosphine were added . The mixture was kept at room temperature overnight, quenched with methanol and evaporated to dryness . The residue was purified by column chromatography (silica-gel ; hexane/dichloromethane 1/1) to yield 9.35 g (75 %) of pure **S** as a white crystal (m.p. 93 °C).[7]

The reactions of **S** with L-CH_2-NH-CH_2-L reagents (iii) as well as the (iv) and (v) steps have been realized by classical procedures .



(i) : $PhCH(OMe)_2$; p.$MeC_6H_4SO_3H$; DMF ; 50°C ; 5hrs (yield : 85%)

(ii) : CBr_4 ; PPh_3 ; DMF ; overnight (yield : 75%)

(iii) : L-CH_2-NH-CH_2-L ; NaH ; CH_2Cl_2 ; 2 days (for instance : 86% with L = 2-pyridyl)

(iv) : HBF_4 (35% in H_2O)-MeCN; 4hrs (quantitative yield)[8]

(v) : one pot : 1) $SOCl_2$; 2) L'-CH_2-NH-CH_2-L'; 2 to 4 days; (yield : 32 and 60% with L' = 2- hydroxyphenyl[9] and 2,3-dihydroxyphenyl respectively, in the case of L = 2-pyridyl)

Scheme 2

It must be emphasized that the yield of (v) is largely improved when using hydroxy-protected phenol groups . Spectroscopic data for 4 (L = 2-pyridyl) and 5 (L = 2-pyridyl ; L' = 2-hydroxyphenyl) are reported herein [8,9] . Other target products obtained in (v) will be described further .

The synthon S and the general synthetic strategy depicted in this paper may allow the syntheses of various dinucleating ligands bearing two chemically distinct co-ordination environments . These ligands are of great interest, since "in dinuclear transition bio-sites, the metal ions are often found in chemically distinct environments" [10] . Very recently, a ligand of this type has been described, which has been prepared with another procedure[11] . The preparation and the characterization of various dimetallic complexes of the ligands synthesized herein are in progress .

References and notes

1. Sanders-Loehr J., Wheeler W.D., Shiemke A.K., Averill B.A.,Loehr T.M. *J.Am.Chem.Soc.* **1989**, *111*, 8084-8093.
2. Martell A.E. *Adv. Supramolecular Chem.* **1990**, *1*, 145-197.
3. Lippard S.J. *Angew.Chem., Int. Ed. Engl.* **1988**, *27*, 344-361.
4. Kurtz D.M. *Chem.Rev.* **1990**, *90*, 585-606.
5. Wieghardt K. *Angew.Chem., Int. Ed. Engl.* **1989**, *28*, 1153-1172.
6. Sorrell T.S. *Tetrahedron* **1989**, *45*, 3-68.
7. synthon S ; *m/z* 320 (MH^+), 319 (M^+), 239, 214 ; *IR* (KBr) 2880, 1470, 1380, 1240, 1210, 950 cm^{-1}; ^1H *NMR* ($CDCl_3$) δ 7.64 (m, 2H), 7.44 (m, 3H), 7.06 (s, 1H), 6.78 (s, 1H), 6.03 (s, 1H), 5.03 (dd,2H), 4.52 (dd, 2H), 2.27 (s, 3H) ; ^{13}C $\{^1H\}$*NMR* ($CDCl_3$) δ 148.7, 136.99, 130.48, 129.81, 129.3, 128.42, 126.33, 125.89, 125.40, 120.93, 98.91, 66.45, 27.77, 20.54 .
8. compound 4 (L = 2-pyridyl) is a brown oil with : *m/z* 349, 257, 239, 198, 93 ; *IR* (film) 3200, 2900, 1582, 1560, 1470, 1420 cm^{-1}; ^1H *NMR* ($CDCl_3$) δ 11.3 (br s, 1 H), 8.56 (dd, 2H), 7.62 (dt, 2H), 7.31 (d, 2H), 7.16 (dt, 2H), 6.95 (d, 1 H), 6.81 (d, 1H), 4.72 (s, 2H), 3.86 (s, 4H), 3.75 (s, 2H), 3.10 (br s, 1H), 2.29 (s, 3H) ; ^{13}C $\{^1H\}$*NMR* ($CDCl_3$) δ 157.82, 152.82, 148.51, 136.54 , 129.68 , 128.32, 127.66, 127.32, 122.95, 121.96, 61.63, 58.70, 56.46, 20.14 .
9. compound 5 (L = 2-pyridyl ; L' = 2-hydroxyphenyl) is a white powder (mp : 68-70°C) with : *m/z* 561 (MH^+), 362, 332 ; *IR* (KBr) 3084, 2922, 2818, 1594, 1482, 1434, 1254 cm^{-1}; ^1H *NMR* ($CDCl_3$) δ 8.61 (d, 2H), 7.57 (dt, 2H), 7.33 (d, 2H), 7.11 (m, 6H), 6.80 (m, 6H), 3.86 (s, 4H), 3.77 (s, 4H), 3.74 (s, 4H), 2.17 (s, 3H) ; ^{13}C $\{^1H\}$*NMR* ($CDCl_3$) δ 157.99, 156.37, 153.62, 148.85, 136.90, 131.45, 130.81, 130.33, 129.04, 127.82, 123.29, 123.03, 122.94, 122.44, 122.28, 119.42, 116.22, 58.98, 56.91, 56.62, 54.95, 20.29 .
10. Crane J.D., Fenton D.E., Latour J.M., Smith A.S. *J. Chem. Soc. Dalton Trans.* **1991**, 2979-2987.
11. Bernard E., Moneta W., Laugier J., Chardon-Noblat S., Deronzier A., Tuchagues J.P., Latour J.M., *Angew.Chem., Int. Ed. Engl.* **1994**, *33*, 887-889.

(*Received in France* 15 *June* 1994; *accepted* 12 *July* 1994)