Highly enantioselective 1,4-addition of diethylzinc to cyclic enones by chiral diphosphite ligands derived from H_8-binaphthoxy moiety

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Supporting Information

General: All reactions were conducted under an inert atmosphere. Toluene and diethyl ether were distilled from sodium and dichloromethane (CH_2Cl_2) was distilled over P_2O_5. PCl_3 was distilled before use. (*S*)-1,1'-bi-2-naphthol and (*R*)-1,1'-bi-2-naphthol were dehydrated by azeotropic distillation with toluene before use. The following substances were commercially available and were used without further purification: $(CuOTf)_2{\cdot}C_6H_6$, $Cu(OTf)_2$, neat Me_2Zn and Et_2Zn. Enones were purchased from Aldrich Chemical Company and distilled from magnesium sulfate prior to use. (*S*)-2,2'-Dihydroxy-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl {(*S*)-H_8-BINOL} was synthesized via a literature procedure (see Aeilts, S. L.; Cefalo, D. R.; Bonitatebus, P. J., Jr.; Houser, J. H.; Hoveyda, A. H.; Schrock, R. R. *Angew. Chem. Int. Ed.* **2001**, *40*, 1452-1456.)

^{1}H NMR and ^{13}C spectra were recorded on a Varian UI-500 (500 MHz) using $CDCl_3$ or CD_2Cl_2 as solvent and with the residual solvent signal as internal reference ($CDCl_3$,

7.24 and 77.0 ppm; CD_2Cl_2, 5.30 and 54.2 ppm). Data are reported as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz) and integration. Ee values were determined by chiral GLC analysis {Chiraldex A-TA column (50 m x 0.25 mm), Chrial diol column (25 m x 0.25 mm), Chiraldex A-TA column (30 m x 0.25 mm) in comparison with authentic materials}. Gas chromatography-mass spectrometry was performed on Hewlett Packard G1880C GCD. High-resolution mass spectra were recorded by direct injection on a Finnigan MAT 95S instrument using the electrospray chemical ionization technique in its positive or negative mode. Analytical TLC was carried out on Merck (Kieselgel 60F-254) silica gel plates with detection by UV light. Optical rotations were measured on a Perkin-Elmer 241 MC at ambient temperature.

Synthesis of (*S*)-1,1'-bi-2-naphthyl bi{(*S*)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl}diphosphite [(*S*,*S*,*S*)-2]

A solution of (*S*)-2,2'-dihydroxy-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl (882 mg, 3 mmol) in toluene (25 mL) was added in 5 minute to a cooled solution (-60 ºC) of phosphorus trichloride (270 µL, 3 mmol) and triethylamine (860 µL, 6mmol) in toluene (5 mL). The reaction mixture was stirred for 2 h during which the reaction mixture was warmed to room temperature. The reaction mixture was filtered and the filtrate was treated with a solution of Et_3N (290 µL, 2.9 mmol), (*S*)-1,1'-bi-2-naphthol (400 mg, 1.4 mmol), DMAP (40 mg, 327 µmol) in toluene (25 mL) at 0 ºC. After 6 h at room

temperature, the reaction mixture was filtered, concentrated, and purified by chromatography (silica gel, hexane:ethyl acetate 3:1) to give (*S*,*S*,*S*)-**2** (1.42 g, 80%) as white solids. Spectral and analytical data for **2**: ^{1}H NMR (CD_2Cl_2): δ 8.08 (d, *J* = 8.5 Hz, 2H), 7.98 (d, *J* = 8.5 Hz, 2H), 7.56 (d, *J* = 9.0 Hz, 2H), 7.44 (t, *J* = 7.0 Hz, 2H), 7.32-7.20 (m, 6H), 7.01 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.0 Hz, 2H), 6.03 (d, *J* = 7.5 Hz, 2H), 2.82-2.60 (m, 8H), 2.57-2.53 (m, 4H), 2.16-2.07 (m, 4H), 1.80-1.66 (m, 12H), 1.49-1.42 (m, 4H) ppm; ^{13}C NMR (CD_2Cl_2) δ 145.9, 145.5, 138.5, 137.6, 135.0, 134.2, 134.0, 131.0, 130.1, 129.3, 129.1, 128.3, 128.2, 127.6, 127.0, 125.9, 125.2, 122.6, 120.0, 118.9, 118.7, 31.2, 31.1, 29.1, 27.7, 22.7, 22.5 ppm; ^{31}P NMR (CD_2Cl_2) δ 138.4 ppm; HRMS calcd. for $C_{60}H_{52}O_6P_2$: 930.3241, found: 930.3161; $[\alpha]_D^{20}$ = +98.0º (c = 1.0, toluene).

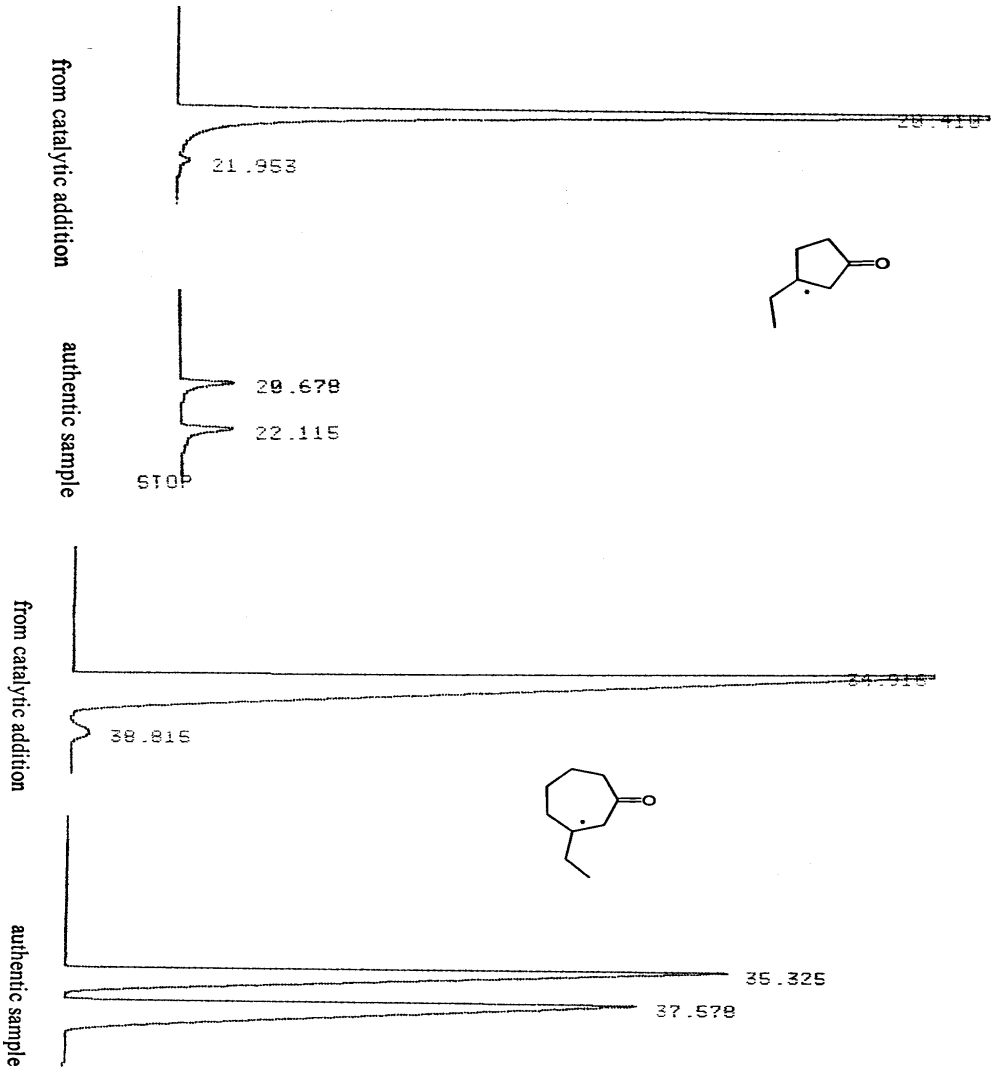
Synthesis of (*R*)-1,1'-bi-2-naphthyl bi{(*S*)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl}diphosphite [(*S*,*R*,*S*)-3]

(*S*,*R*,*S*)-**3** was synthesized in 85% yield via a similar procedure as described above for the preparation of (*S*,*S*,*S*)-**2** and the crude product was purified by column chromatography chromatography (silica gel, hexane:ethyl acetate 3:1). Spectral and analytical data for **3**: m.p. 167 °C; ^{1}H NMR (CD_2Cl_2): δ 8.05 (d, *J* = 9.0 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 2H), 7.49-7.47 (m, 4H), 7.28 (td, *J* = 7.3, 1.5 Hz, 2H), 7.20-7.18 (m, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.73 (d, *J* = 7.0 Hz, 2H), 6.42 (d, *J* = 8.0 Hz, 2H), 5.3 (d, *J* = 8.5 Hz, 2H), 2.71-2.47 (m, 12H), 2.09-2.04 (m, 4H), 1.69-1.61 (m, 12H), 1.45-1.41 (m, 4H) ppm; ^{13}C NMR (CD_2Cl_2): δ 148.4, 145.8, 138.5, 138.1, 137.1, 135.2, 134.2, 134.0, 131.2,

130.3, 129.3, 129.1, 128.8, 128.2, 127.5, 127.1, 126.1, 125.3, 123.1, 121.4, 118.8, 118.5, 29.1, 29.1, 27.8, 27.7, 22.7, 22.7, 22.5, 22.5 ppm**;** ^{31}P NMR ($CDCl_3$): δ 138.3 ppm; HRMS for $C_{60}H_{52}P_2O_6$, calcd: 930.3241, Found: 930.3306; $[\alpha]_D^{20}$ = +91.1° (c = 1.0, toluene).

Representative experimental procedure for the Cu-catalyzed conjugate addition of diethylzinc to cycloalkenones

Reactions were carried out under a nitrogen atmosphere using oven or flame-dried glassware. The catalyst was first generated *in situ* by stirring $(CuOTf)_2{\cdot}C_6H_6$ {or $Cu(OTf)_2$} (1 mol%) and the ligand (2 mol%) in dry Et_2O (2-3 mL) for 20~30 min. To this catalyst solution was added dropwise the cycloalkenone (1.0 equiv.), followed by the addition of dialkylzinc (1.5 equiv.) at –30 - 0 °C. The reaction was allowed to proceed for the time and at the temperature as specified and was quenched by the addition of a saturated aqueous solution of ammonium chloride (1.5 – 2.0 mL). The aqueous layer was extracted with diethyl ether (3 x 2 mL) and the combined extracts were dried ($MgSO_4$), filtered and concentrated in vacuo to afford the crude products as an oil. The yield and the enantioselectivity of the crude products were directly determined by using a GC instrument equipped with a chiral capillary column (AT-A column) in the presence of dodecane as an internal standard. The chromatograms are illustrated below: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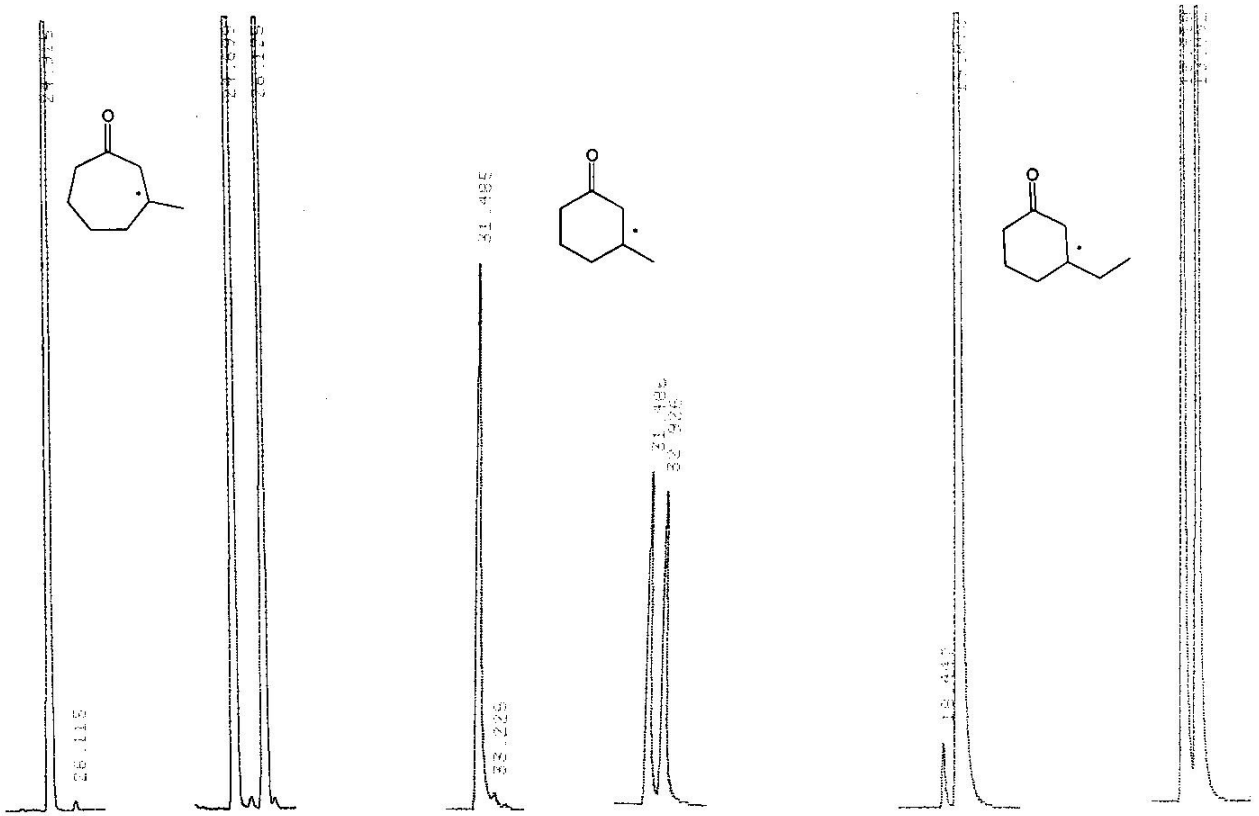
20.678
22.115
STOP
from catalytic addition
38.815
authentic sample
35.325
37.578



from catalytic addition authentic sample from catalytic addition authentic sample from catalytic addition authentic sample

2001524

exp3 s2pul

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file	exp	spin	not used
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at	1.600	alfa	10.000
np	142400	FLAGS	
fb	25000	il	n
bs	64	in	n
d1	1.000	dp	y
nt	64	hs	ny
ct	64	PROCESSING	
TRANSMITTER		lb	1.00
tn	P31	fn	not used
sfrq	202.316	DISPLAY	
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pw	19.444	rfl	4040.1
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dn	H1	rp	-29.7
dof	0	lp	-399.9
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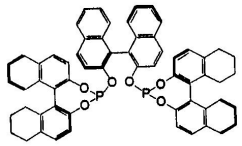
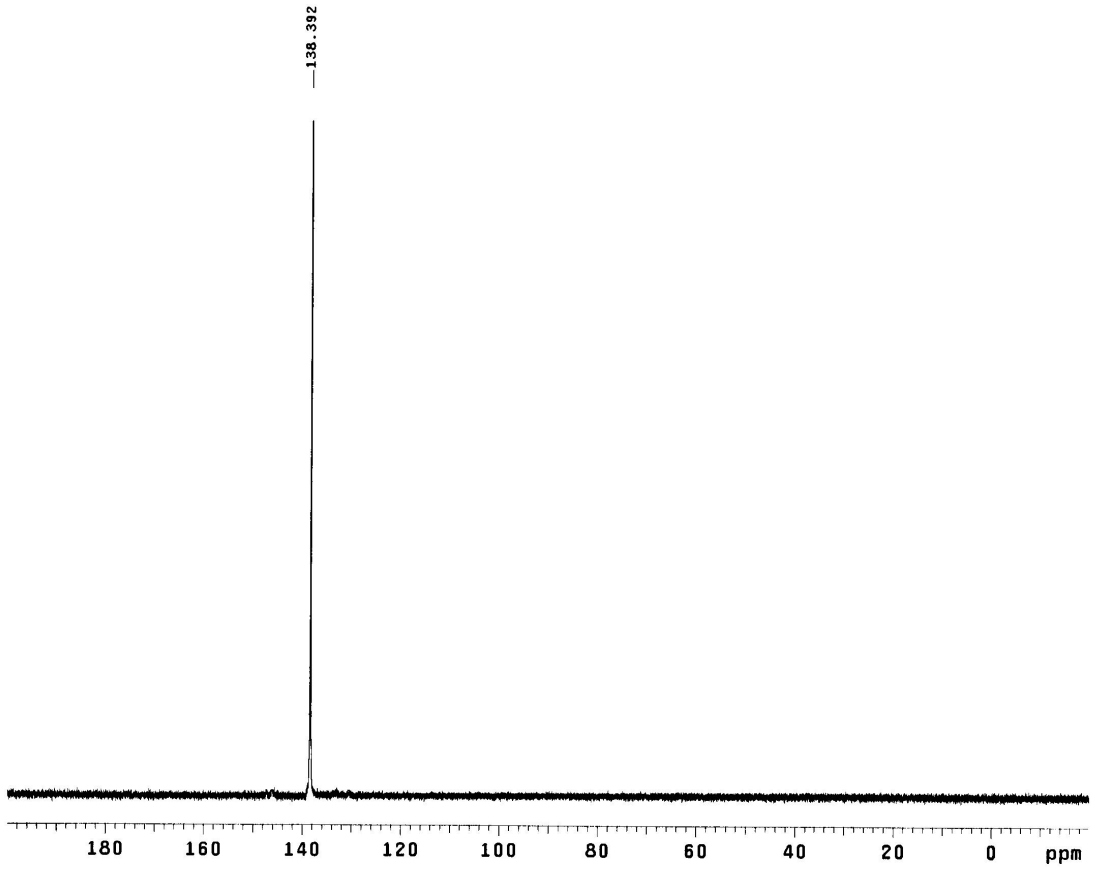
		ai	cdc ph



(*S,S,S*)-2



2001524C

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at	1.043	alfa	10.000
np	65536	FLAGS	
fb	17000	il	n
bs	64	in	n
d1	1.000	dp	y
nt	2000	hs	nn
ct	2000	PROCESSING	
TRANSMITTER		lb	0.50
tn	C13	fn	not used
sfrq	125.673	DISPLAY	
tof	1883.4	sp	2423.8
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pw	11.400	rfl	1882.1
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dn	H1	rp	5.3
dof	0	lp	-190.5
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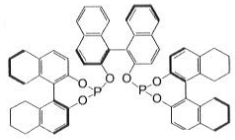
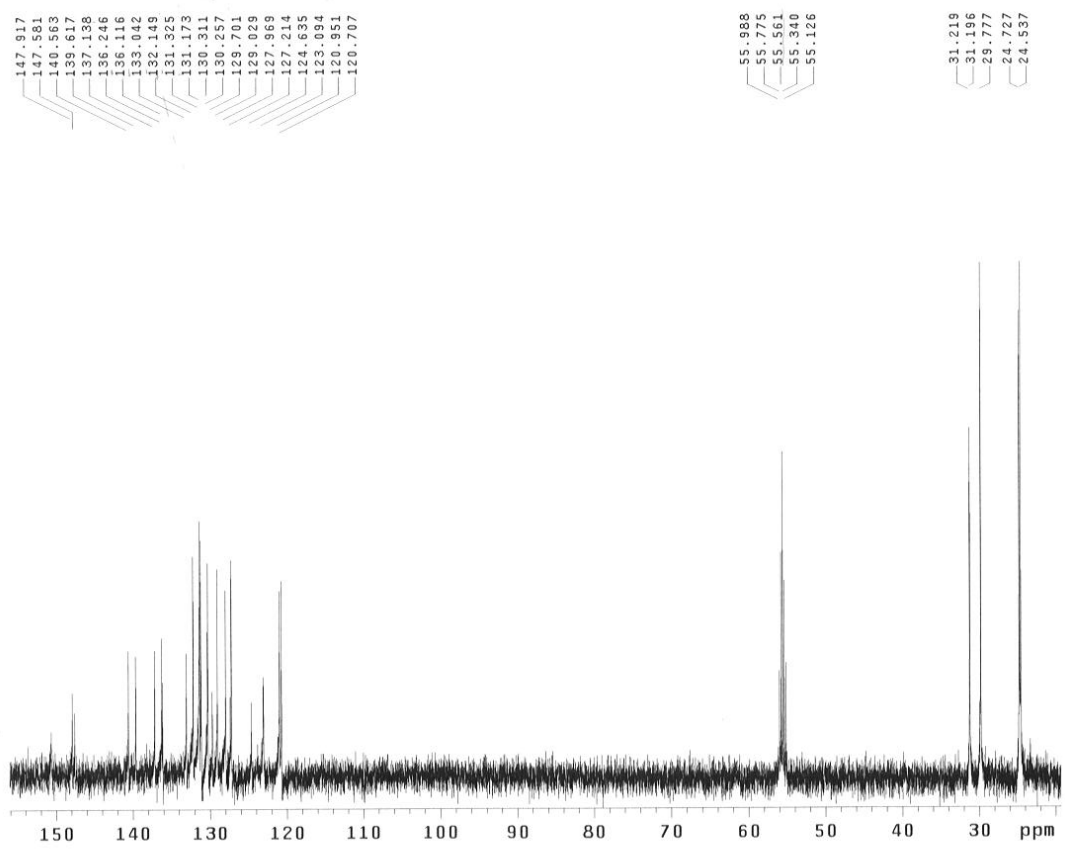


(*S,S,S*)-2



2001524H

exp3 s2pul

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at	2.049	alfa	0
np	32768	**FLAGS**	
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bs	32	in	n
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ct	16	**PROCESSING**	
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tn	H1	**DISPLAY**	
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dn	C13	lp	-23.9
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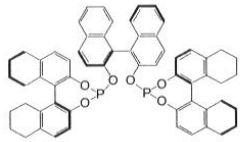
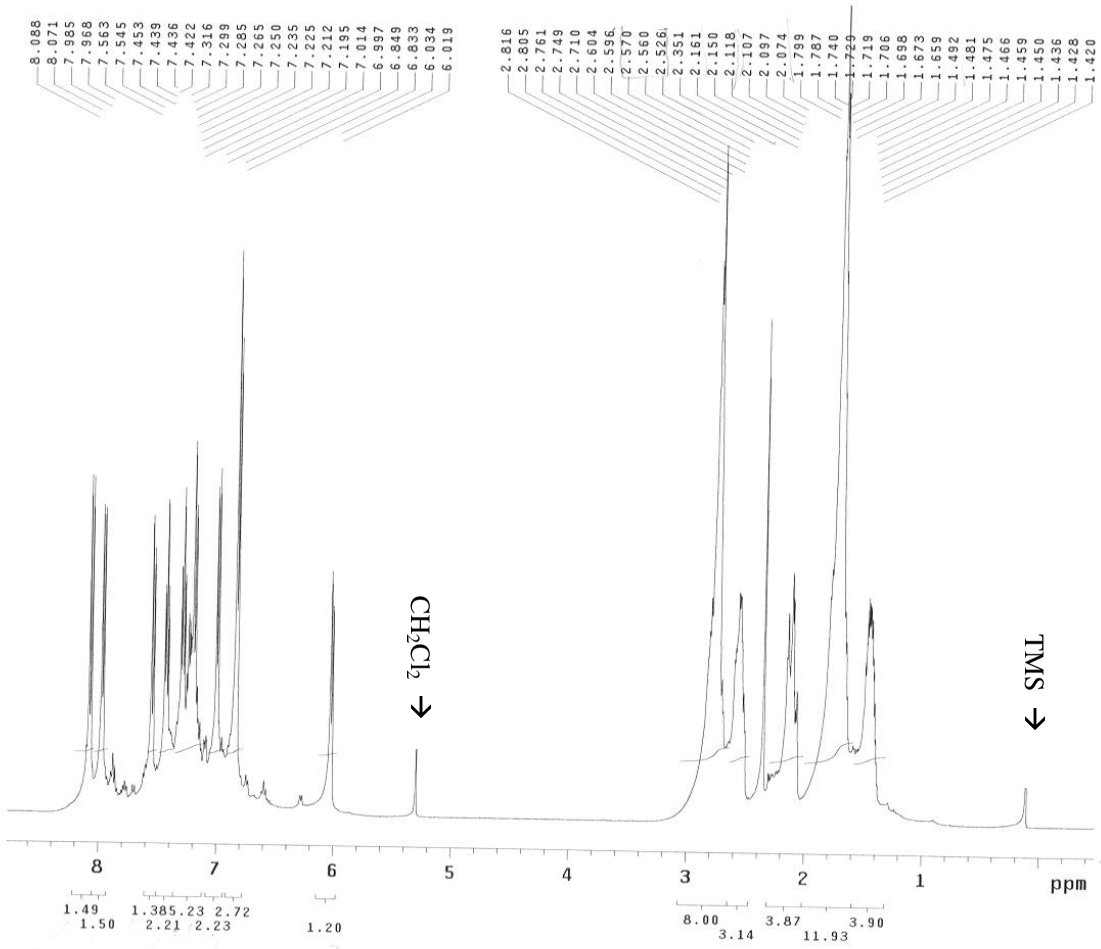


(*S*,*S*,*S*)-2



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ENYLPHOSPHATE PARAMETERS

31

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      exp   spin       not used
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   142400          FLAGS
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       64    in             n
    1.000    dp             y
       64    hs            ny
       64       PROCESSING
ITTER        lb          1.00
      P31    fn      not used
  202.317       DISPLAY
  23275.8    sp       -4040.1
       63    wp       44493.9
   19.444    rfl       4040.1
PLER         rfp             0
       H1    rp           12.5
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             ai  cdc  ph
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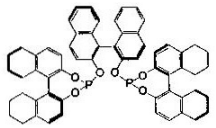
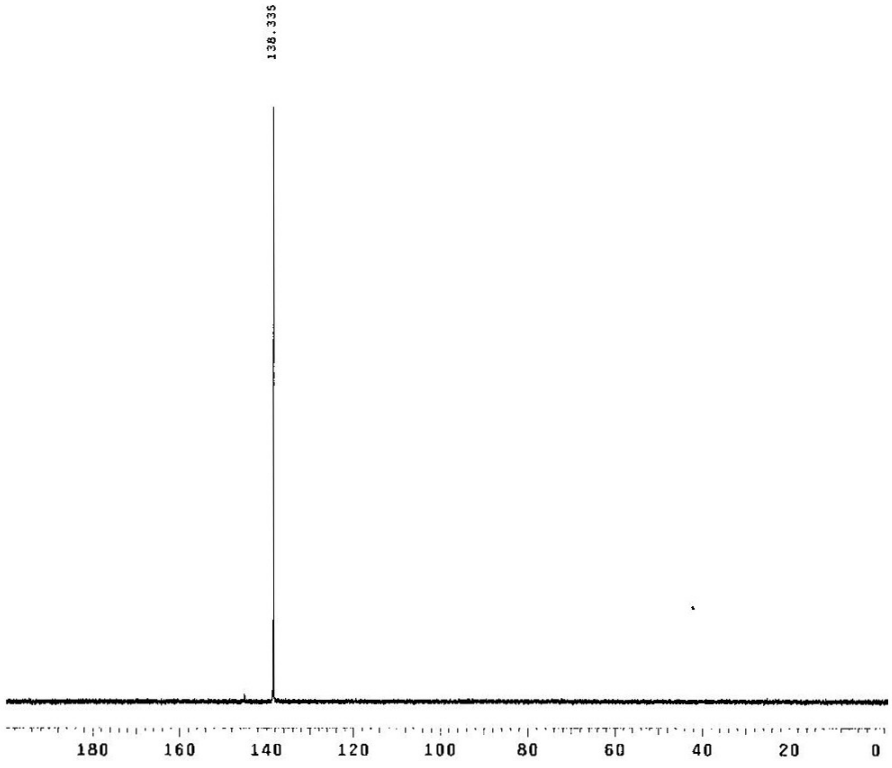


(*S,R,S*)-**3**



urity		
l		
LE	SPECIAL	
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1.043	alfa	10.000
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64	in	n
1.000	dp	y
2000	hs	nn
1920	PROCESSING	
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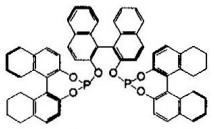
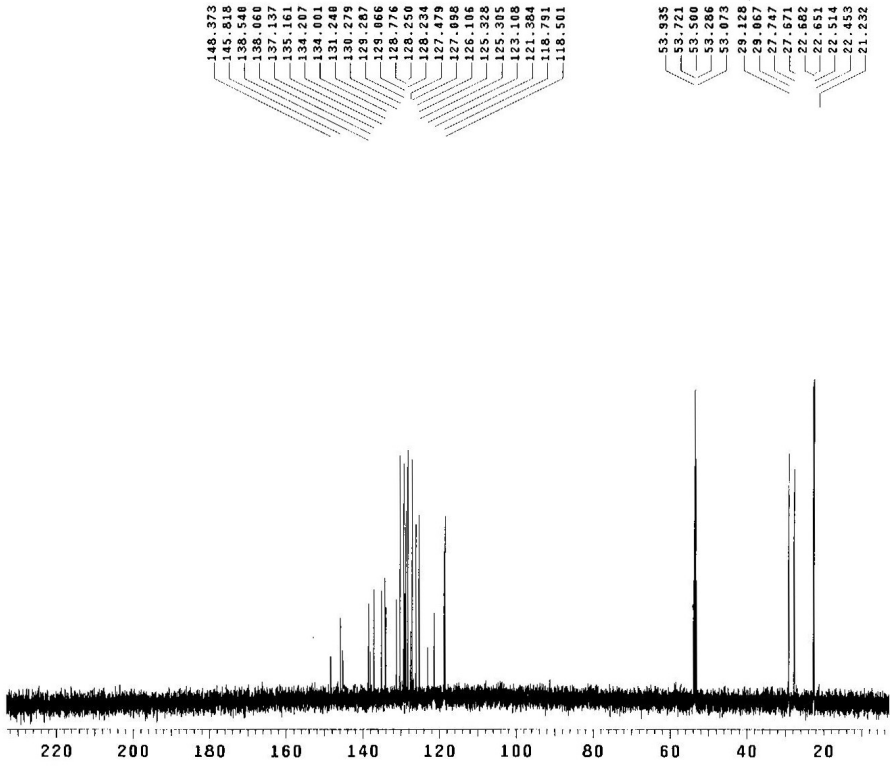
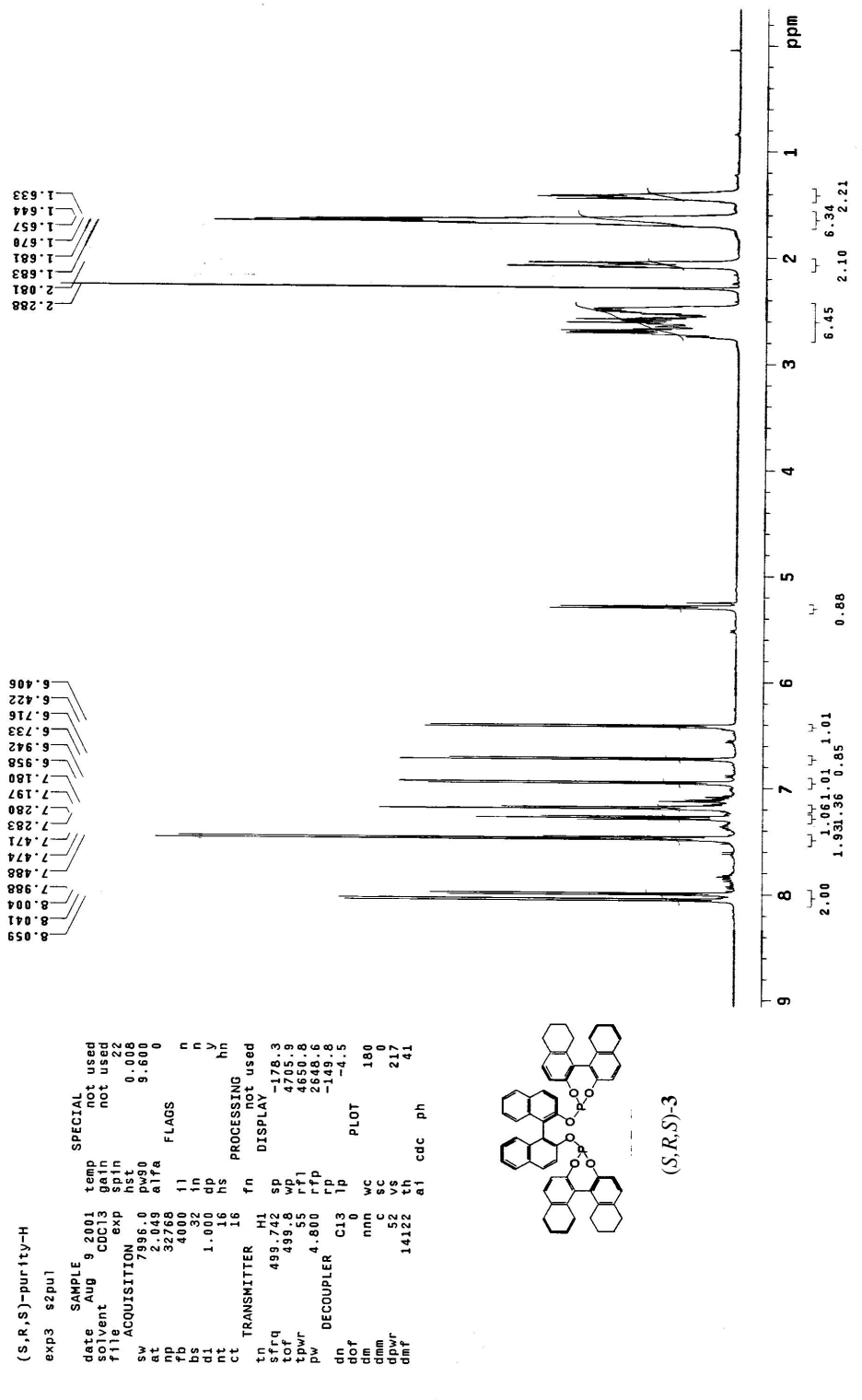


(*S*,*R*,*S*)-**3**

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2.21

(*S*,*R*,*S*)-**3**