N, 2.00. Found: C, 60.03; H, 8.22; N, 1.98.

Registry No. 1, 64743-16-4; 3, 81692-79-7; 4, 81686-47-7; 5, 81686-48-8; 6, 81738-68-3; 7, 81738-69-4; 8, 83349-69-3; 9, 83349-70-6; 10, 81767-43-3; 11, 81686-49-9; 12, 81767-44-4; 13, 81686-50-2.

Selective Alkylations of Phenolic Ketones

Donald R. Dimmel* and Donaline Shepard

The Institute of Paper Chemistry, Appleton, Wisconsin 54912

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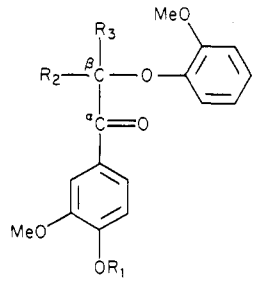
Lignin models are often used in mechanistic studies in an attempt to understand the chemistry of native lignin, a complex, random, cross-linked polymeric component of wood.[1] We describe a new synthesis of lignin models, one which allows the introduction of β-substituents (1) without having to protect[2] the phenolic hydroxyl group. The method takes advantage of a selective alkylation of a dianion.



1a, $R_1 = R_2 = R_3 = H$
b, $R_1 = R_2 = Li$; $R_3 = H$
c, $R_1 = R_2 = H$; $R_3 = Me$
d, $R_1 = R_2 = Li$; $R_3 = Me$
e, $R_1 = H$; $R_2 = R_3 = Me$
f, $R_1 = R_2 = H$; $R_3 = CH_2OH$

A sample of **1a**[3] was treated with an excess of lithium diisopropylamine (LDA), followed by addition of excess methyl iodide (MeI) and then acid, to afford a mixture of starting ketone (**1a**) and monomethylated ketone **1c**. The two ketones were easily separated by column chromatography. The presumed intermediate formed by LDA treatment was the dilithiospecies **1b**, which apparently only alkylated at the β-carbon. The low reactivity of the lithium phenolate group was surprising; both phenol and guaiacol (*o*-methoxyphenol) were also not alkylated with this LDA/MeI treatment. These results suggest that phenols do not have to be protected (i.e., a benzyl ether) prior to base-induced alkylations involving LDA.

The monomethylated ketone **1c** could be converted via **1d** to a mixture of **1c** and dimethylated ketone **1e** by LDA/MeI treatment. Again, the two ketones were easily separated by chromatography.

In an attempt to define the scope of these alkylations, we treated the dilithio species **1b** with a variety of alkylating agents, including ethyl, propyl, and benzyl halides and formaldehyde. Only the latter reaction was successful, producing **1f**. Although extensive variations of reaction conditions were not examined, it appears that the alkylation of **1b** is restricted to some simple, unhindered electrophiles. Two variations which were examined, employing *n*-butyllithium alone as the base and LDA/MeI treatment of the acetate of **1a**, gave methylated product but in lower conversion than the typical procedure.

Experimental Section

The instrumentation used has been described previously.[4] All melting and boiling points are uncorrected.

General Alkylation Procedures. All alkylations employed dried glassware, anhydrous solvents, distilled reagents, and a nitrogen atmosphere. To 100 mL of ice-cooled, stirred tetrahydrofuran (THF) was added 4 equiv of *n*-butyllithium in hexane, followed by 4 equiv of diisopropylamine. After being stirred 15 min, the solution was cooled to −70 °C, and 1 equiv of ketone (about 50 mmol) dissolved in THF was added dropwise. The stirred mixture was then allowed to warm to room temperature for 1 h, followed by cooling again to −70 °C. The alkylating agent (4 equiv), generally an alkyl halide, was dissolved in THF and added dropwise. In the case of formaldehyde, a separate vessel containing dry paraformaldehyde was pyrolyzed at 200 °C and an excess amount of the gaseous reactant swept into the reaction flask with a stream of nitrogen. After addition of the alkylating agent, the mixture was stirred for several hours at room temperature.

The reaction mixture was quenched by the addition of aqueous NH_4Cl. The organic layer was separated and the aqueous layer extracted several times with fresh ether. (If emulsions developed, dilute HCl was added.) The combined organic extracts were washed with 3 M HCl and then twice extracted with 1 M NaOH. The alkaline extracts were acidified and extracted three times with ether. The combined ether extracts were dried (Na_2SO_4) and evaporated to afford the crude product, which by ^1H NMR analysis was generally a simple mixture of starting and product ketones.

The crude product was purified by chromatography on a silica gel column with first 600 mL of toluene and then successive 400-mL increments of 10%, 20%, 30%, and 40% ether–toluene over about a 6-h period. The order of elution was β,β-dimethyl ketone **1e**, β-methyl ketone **1c**, unsubstituted ketone **1a**, and β-hydroxymethyl ketone **1f**. Fractions of desired ketone were combined and recrystallized.

1-(4-Hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-1-propanone (1c). The methylation to produce this compound was done several times with varying reactant levels. As an example of a somewhat large scale run, 217 mL of 1.6 M *n*-butyllithium in hexane, 48.7 mL of diisopropylamine, 25 g of **1a**, 21.6 mL of methyl iodide, and roughly 300 mL of THF afforded 27.6 g of crude product which by NMR was roughly a 2:1 mixture of **1c**/**1a** containing small amounts of solvent. Chromatography gave pure **1c**: mp 131–133 °C (benzene–petroleum ether); ^1H NMR and mass spectral data agreed with literature values.[2a,b] In general, the conversion of **1a** to **1c** was 50–65%.

1-(4-Hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-2-methylpropanone (1e). The conversion for **1c** to **1e** was roughly 33%. Consequently, the product of one methylation was used as the starting material for another until the product mixture was rich in the **1e** component. Chromatography afforded pure **1e**: mp 98–100 °C (benzene–petroleum ether); IR (mull) 2900–3500 (OH), 1760 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 1.65 (s, 6, Me), 3.76 (s, 3, OMe), 3.89 (s, 3, OMe), 6.09 (s, 1, OH), 6.7–6.9 (m, 5, aryl), 7.8–8.2 (m, 2, aryl); ^{13}C NMR ($CDCl_3$) 26.1 (q, Me), 55.4 (q, OMe), 56.0 (q, OMe), 86.0 (s, C_2), 112.2 (d), 112.4 (d), 113.8 (d), 120.3 (d), 120.6 (d), 123.0 (d), 125.8 (d), 127.5 (s), 144.5 (s), 146.0 (s), 149.9 (s) and 151.6 (s) (aryl), 200.1 ppm (s, C_1); MS, *m/e* (relative intensity) 316 (9, M^+), 165 (100), 151 (16), 125 (16), 124 (28), 123 (13).

3-Hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-1-propanone (1f). This reaction was only per-

(1) Sarkanen, K. V.; Ludwig, C. H., Eds. "Lignins"; Wiley-Interscience: New York, 1971.
(2) The following are examples: (a) Adler, E.; Delin, S.; Miksche, G. E. *Acta Chem. Scand.* **1966**, *20*, 1035. (b) Omori, S.; Dence, C. W. *Wood Sci. Technol.* **1980**, *15*, 67.
(3) Hosoya, S.; Kanazawa, K.; Kaneko, H.; Nakano, J. *Mokuza Gakkaishi* **1980**, *26*, 118.
(4) Dimmel, D. R.; Shepard, D.; Brown, T. A. *J. Wood Chem. Technol.* **1981**, *1*, 123.

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formed once. The yield was somewhat low, but the conversion (based on NMR) was high (roughly 90%). Chromatography gave pure **1f**: mp 78–80 °C (MeOH–H_2O); ^1H NMR and mass spectral data agreed with literature values.[2b]

Registry No. **1a**, 22317-35-7; **1c**, 7107-93-9; **1e**, 83248-99-1; **1f**, 22317-34-6.

A Spectroscopic Method for the Determination of Optical Purities of Chiral, Chelating Diphosphines

Evan P. Kyba* and Steven P. Rines

Department of Chemistry, The University of Texas at Austin, Austin, Texas 78712

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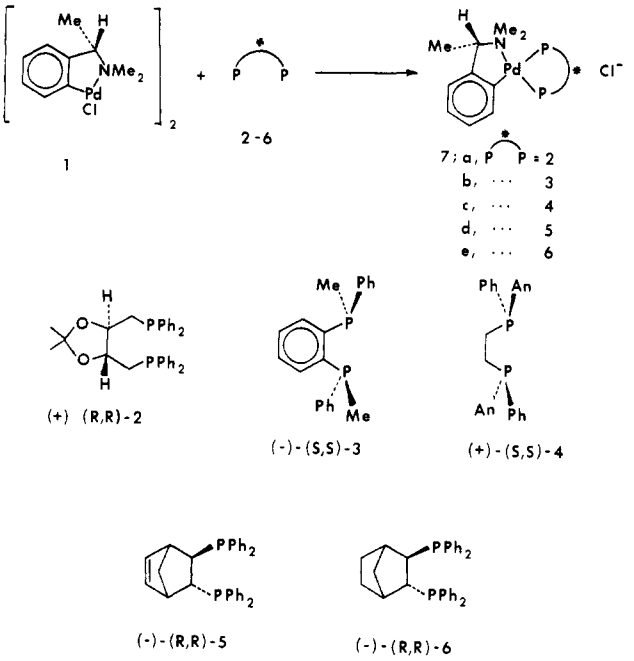
In the past decade there has been a rapid expansion of activity in the area of asymmetric catalytic hydrogenation of prochiral olefins mediated by Rh(I) complexes of chiral, chelating diphosphines.[1] This effort has involved mechanistic work,[2] as well as the design and synthesis of new chiral diphosphines to be tested for their efficacy in asymmetric induction during catalytic hydrogenation.[3]

The synthesis of optically active diphosphines can involve the elaboration of an optically active purcursor[3a-e,g] or the preparation of racemic diphosphines or their dioxides, followed by resolution of the dioxides[3f] or resolution of the diphosphines.[3h,4] Although it would be very useful to have a general spectroscopic method for the evaluation of the optical purity of any chiral disphosphine, to our knowledge such a technique has not been reported. In this note we describe and illustrate such a method.

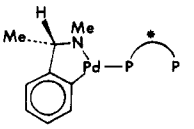
The diphosphine complexes (**7**, Scheme I) were formed in situ from (−)-bis(μ-chloro)bis[(*R*)-dimethyl(α-methylbenzyl)aminato-C^2,*N*]dipalladium(II) (**1**)[3h,4,5] and the corresponding diphosphines **2–6** by dissolving the two reagents in $CDCl_3$ in a molar ratio of 0.50:1.0, respectively, to give ca. 0.1 M homogeneous, straw-yellow solutions. Both ^{31}P and ^1H NMR spectra were recorded on these solutions. Either one optically pure ligand was used, followed by the addition of the antipode, along with a concomitant increase in the amount of **1** (with **2**, **3**, **5**, and **6**), or one enantiomer was run, followed by another run on a racemic mixture (with **4**[6]). Pertinent NMR spectroscopic data are presented in Table I.

Scheme I



It is apparent that in each of the five cases studied, this spectroscopic method can be used to determine optical purity. In principle, one would expect at least a pair of doublets in the ^{31}P NMR spectrum for each optically pure ligand, since the phosphorus atoms trans to nitrogen should be chemically different from those trans to carbon, and coupled. This was found to be true for ligands **3** and **4**, but since the two phosphino sites in **5** and **6** are chemically different (exo and endo) two complexes of each enantiomer are formed (85:15 with **5** and 97:3 with **6**). The chemical shifts of these species are sufficiently different that no difficulty was experienced in determining diastereomeric ratios, and thus optical purities.

In contrast to the ^{31}P NMR spectra of **7b–e**, which all feature pairs of doublets, **7a** exhibits only a singlet for each diasteriomeric complex. A priori, this could be due to fortuitous ^{31}P chemical shift equivalence of the phosphorus atoms in each diastereomeric complex (**7a**) or to rapid site–site exchange of the two phosphino ligands. The ^{31}P NMR signal remained sharp for **7a** down to −90 °C, indicating that if the latter case obtains, the mechanism for achieving equivalence has a low activation barrier. Presumably, such a mechanism would involve decoordination of one of the chelating phosphines to form a tricoordinate species such as **8** followed by recoordination trans to either



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the nitrogen or carbon ligand. Evidence for the facility of the deligation/religation sequence with six-membered chelates of Rh(I) has been presented by Collman.[7] Consistent with this notion is our observation that the reaction of (−)-**3** with **7a** to give **7b** and (+)-**2** is rapid and quan-

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(2) (a) Brown, J. M.; Parker, D. *J. Chem. Soc., Chem. Commun.* **1980**, 342. (b) Brown, J. M.; Chaloner, P. A. *Ibid.* **1980**, 344. (c) Brown, J. M.; Chaloner, P. A. *J. Am. Chem. Soc.* **1980**, *102*, 3040. (d) Chan, A. S. C.; Pluth, J. J.; Halpern, J. *Ibid.* **1980**, *102*, 5952. (e) Chan, A. S. C.; Halpern, J. *Ibid.* **1980**, *102*, 838. (f) Ojima, I.; Kogure, T.; Yoda, N. *J. Org. Chem.* **1980**, *45*, 4728. (g) Ojima, I.; Kogure, T.; Yoda, N. *Chem. Lett.* **1979**, 495. (h) Ojima, I.; Kogure, T.; Yoda, T. *Ibid.* **1979**, 641. (i) Achiwa, K.; Ohga, Y.; Iitaka, Y.; Saita, H. *Tetrahedron Lett.* **1978**, 4683.

(3) A recent review[1a] contains an extensive catalog of chiral diphosphines. The following references represent key papers in the field. (a) Kagan, H. B.; Dang, T.-P. *J. Am. Chem. Soc.* **1972**, *94*, 6429. (b) Vineyard, B. D.; Knowles, W. S.; Sabacky, M. J.; Bachman, G. L.; Weinkauff, D. J. *Ibid.* **1977**, *99*, 5946. (c) Fryzuk, M. D.; Bosnich, B. *Ibid.* **1977**, *99*, 6262. (d) Fryzuk, M. D.; Bosnich, B. *Ibid.* **1978**, *100*, 5491. (e) Achiwa, K. *Ibid.* **1976**, *98*, 8265. (f) Brunner, H.; Pieronczyk, W. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 620. (g) Lauer, M.; Samuel, O.; Kagan, H. B. *J. Organomet. Chem.* **1979**, *177*, 309. (h) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932. (i) Kyba, E. P.; Davis, R. E.; Juri, P. N.; Shirley, K. N. *Inorg. Chem.* **1981**, *20*, 3616.

(4) Roberts, N. K.; Wild, S. B. *J. Am. Chem. Soc.* **1979**, *101*, 6254.

(5) Roberts, N. K.; Wild, S. B. *J. Chem. Soc., Dalton Trans.* **1979**, 2015.

(6) We are most grateful to Dr. Karl Koenig of Monsanto for a generous gift of optically active and racemic **4**.

(7) Siegel, W. O.; Lapporte, S. J.; Collman, J. P. *Inorg. Chem.* **1971**, *10*, 2158.

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