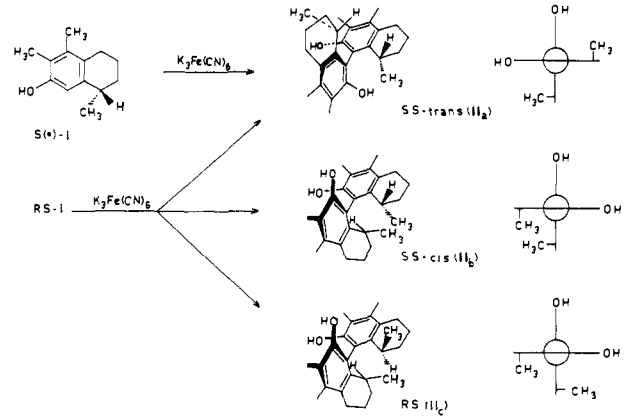
A Stereospecific Phenol Coupling Reaction

Sir:

Phenolic oxidative coupling has long been considered as one of the important steps in the biosynthesis of many natural products.[1] Although the oxidation of phenolic compounds with a variety of chemical[2] and biological oxidants[3] has been studied, little is known about the stereochemical course of this reaction.[4]

We wish to report the stereospecific oxidative dimerization of a model phenol and indication of the formation of an intermediate complex. The remarkable stereospecificity of the reaction is apparently caused by the presence of one asymmetric center in the model compound (I). When a solution of optically pure (*S*)-(+)-7-hydroxy-1,5,6-trimethyl-1,2,3,4-tetrahydronaphthalene (I) (0.235 g, 1.23 mmol, $|\alpha|_{578}$ +14.8°, *c* 0.3, ethanol)[5,6] in 43 ml of diethyl ether was stirred for 2 h with a solution of $K_3Fe(CN)_6$ (0.448 g, 1.44 mmol) in 18.5 ml of 0.2 N NaOH at 20 °C; 0.141 g (0.386 mmol, 62.9%) of dimer (one pure isomer)[7] could be isolated by preparative TLC (Scheme I). This optically active dimer (mp 173–174°, $|\alpha|_{578}$ +10.5; $|\alpha|_{365}$ 0° (both *c* 0.5, ethanol) shows one doublet at δ 0.72 ppm for the protons of the C_1,C_1'-methyl groups in the 100-MHz ^{1}H NMR. The ORD and CD spectra of this dimer showed a negative Cotton effect at 278 nm corresponding to the ^1L_b uv band, a positive 225-nm ^1L_a band Cotton effect, and probably a short wavelength negative Cotton effect centered at the ^1B_a band (180–190 nm) (Figure 1). The positions of the ORD and CD extrema were very similar in the dimer and the monomer. Mislow and co-workers[8] investigated a series of chiral biaryl compounds and correlated the biaryl configurations with the sign of the Cotton effects. Theoretical treatment by Mason and co-workers[9] and Hug and Wagniere[10] were consistent with these results. According to the rules of the authors cited above[8-10] and the results of the configurational correlation by ORD and CD in the lythraceae alkaloids series,[11] a positive ^1L_a Cotton effect indicates the (*S*)-biaryl configuration, and therefore the dimer must be the (*SS*)-*trans*-II_a enantiomer. Although the substituent influence on the aromatic chromophore is uncertain, a negative ^1L_b Cotton effect probably indicates a cis conformation of the biaryl moiety. The results indicate that the oxidative coupling of (*S*)-(+)-I monomer gives the least sterically hindered (*SS*)-*trans*-II_a enantiomer in a completely stereospecific manner.

Scheme I. Oridative Coupling of (*S*)-(+)-I and (*RS*)-I



A second remarkable feature of this reaction is the finding that oxidation of racemic I (RS-I) furnished a mixture of three diastereomeric *dl*-dimers in the same yield (62%).

The ratios of these three dimers (see Scheme I) are II_a:II_b:II_c as 66.0:7.9:26.1.[12]

The 100-MHz ^{1}H NMR spectrum of this mixture shows two doublets of the same intensity at δ 0.96 ppm and δ 0.81 ppm for the protons of the C_1,C_1'-methyl groups of the *RS*-pair (II_c). Furthermore a doublet at δ 0.83 ppm due to the protons of the C_1,C_1'-methyl groups of the *SS* (*RR*)-cis pair (II_b) and a doublet at δ 0.72 ppm for the corresponding protons of the *SS* (*RR*)-trans isomers (II_a). Models of the three isomers show subtle but definite differences in the extent by which the protons of the pseudo-axial oriented C_1,C_1'-methyl substituents are influenced by the shielding zones of the aromatic rings. The identification of the dimer II_a as the major product is based upon these differences as evidenced by the proton absorptions of the C_1,C_1'-methyl groups in the 100-MHz ^{1}H NMR spectrum.

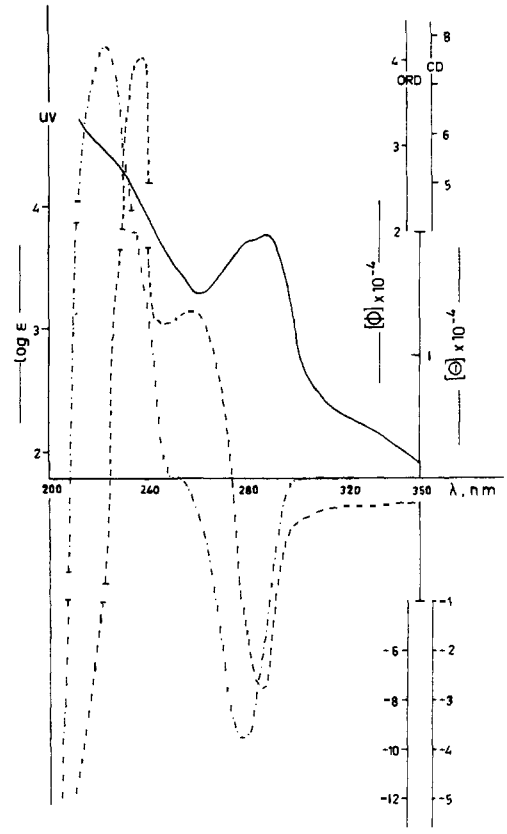


Figure 1. Uv (—), ORD (- - -), and CD (• • •) spectra of (*SS*)-*trans*-II_a (95% ethanol).

According to the 100-MHz ^{1}H NMR spectrum, the dimer of the (*S*)-(+)-I coupling is the (*SS*)-*trans*-II_a enantiomer in agreement with the configurational assignment based on the chiroptical properties mentioned above.

The extent of the stereospecificity of the biaryl coupling of (*RS*)-I can be interpreted from the product distribution (Scheme I). Since the (*SS*)-trans and (*SS*)-cis isomers differ only in the biaryl configuration the diastereospecificity of this oxidation is 80%.

It is unexpected that a mixture of diastereoisomers is formed when (*RS*)-I is dimerized (with 7.9% (*SS*)-*cis*-II_b) while the dimerization of optically pure (*S*)-(+)-I proceeded in an apparently totally stereospecific manner. The conclusion is inescapable, that one enantiomer influences the stereochemical course of the dimerization of the other enantiomer. This could be visualized via diastereomeric complexes.[13] Furthermore, it is noteworthy that asymmetry in the starting phenol (I) at one chiral center (at C_1) appears sufficient to cause this high stereospecificity. Few examples are known in which an optically active phenol coupling product isolated from a natural product, contains no other chiral centers than its own biaryl dissymmetry.[14] Since the biosynthetic pathways to these diphenols have not been entirely elucidated chiral precursors to the final product are not excluded. Further investigations of

the stereochemistry of the phenol oxidation reactions are in progress.

References and Notes

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(2) (a) H. Musso, *Angew. Chem.*, **75**, 965 (1963); (b) P. D. McDonald and G. A. Hamilton, In "Oxidation in Organic Chemistry", Part B, W. S. Trahanovsky, Ed., Academic Press, New York, N.Y., 1973, Chapter 2; (c) M. A. Schwartz, R. A. Holton, and S. W. Scott, *J. Am. Chem. Soc.*, **91**, 2800 (1969); (d) M. A. Schwartz, B. F. Rose, and B. Vishnuvajjala, *ibid.*, **95**, 612 (1973).

(3) B. R. Brown in ref 1b.

(4) To our knowledge Bobbitt's electrochemical oxidation of a tetrahydroisoquinoline is the first and only example of an investigation into the stereospecificity of the phenol coupling reaction. J. M. Bobbitt, J. Noguchi, H. Yagi, and K. H. Weisgraber, *J. Am. Chem. Soc.*, **93**, 3551 (1971).

(5) Optically active phenol (*S*)-(+)-I was prepared by standard methods from optically active 1-carboxy-5,6-dimethyl-7-hydroxy-1,2,3,4-tetrahydronaphthalene ((*S*)-(−)-III). The latter compound was resolved through its 1-(+)-dehydroabietylamine salts and the optical purity of (*S*)-(+)-I, determined by examination of the 100-MHz ^{1}H NMR spectrum of the 1-(−)-α-phenylethylamide of III was > 97.5%. The configurations of (*S*)-(−)-III and (*S*)-(+)-I were independently correlated using the ORD and CD Cotton effects, with the unsubstituted 1-methyl- and 1-carboxytetralins of known absolute configurations;[5a] substituent influences were determined by helicity- and sectorrules for the ^1L_b transition.[5b] (a) J. Barry, H. B. Kagan, and G. Snatzke, *Tetrahedron*, **27**, 4737 (1971); B. Sjoberg, *Acta Chem. Scand.*, **14**, 273 (1960); (b) G. Snatzke, M. Kajtar, F. Snatzke in "Fundamental Aspects and Recent Developments in Optical Rotatory Dispersion and Circular Dichroism", F. Ciardelli and P. Salvadori, Ed., Heyden & Sons, London, New York, Theime, 1973, Chapter 3.4.

(6) All new compounds gave satisfactory elemental analysis and spectral data in agreement with the structure.

(7) The entire crude dimer fraction, without purification, was examined minutely using 100-MHz ^{1}H NMR, TLC, and HPLC. Only dimer II_a was found to be present. No trace of dimer II_b could be detected. Since we had been able to detect this dimer II_b in 8% quantities in the more complex mixture, we feel certain about its absence in this case.

(8) K. Mislow, *Top. Stereochem.*, **4**, 1–42 (1968).

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(12) (a) Both reactions (coupling of (*S*)-(+)-I and of (*RS*)-I) were run under identical conditions including a completely quantitative (nonfractionating) workup. The entire dimer fraction, isolated via preparative TLC, was first subjected to a careful NMR analysis prior to further purification. This fraction showed a correct total elemental analysis. The 100-MHz ^{1}H NMR spectrum uniquely identifies the three *dl*-pairs. In addition complete separation was achieved via HPLC (Waters Liquid Chromatograph, column 50 cm × 3/8, Si 60-5, Prop. Cl, hexane 1:1) and *all* three diastereomeric dimers were individually identified (exact mass determination). All other spectral data of the individual diastereomers were obtained.

(13) We will not at this time try to speculate whether or not such a complex incorporates part of the $K_3Fe(CN)_6$ moiety.

(14) See, for example, the elegant work by S. Shibata and co-workers on the Ustilaginoidins. S. Shibata, *Chem. Brit.*, **3**, 110 (1967).

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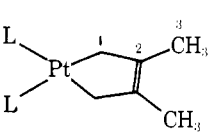
Organoplatinum Complexes Related to the Cyclodimerization of 1,3-Dienes. Reactions of 2,3-Dimethylbuta-1,3-diene and Buta-1,3-diene with Bis(cycloocta-1,5-diene)platinum or Bis(ethylene)trimethylphosphineplatinum

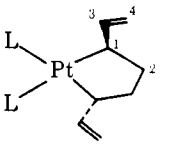
Sir:

The discovery and development of the nickel(0) catalyzed cyclodimerization and cyclotrimerization reactions of 1,3-dienes rank as one of the major achievements of organometallic chemistry.[1] Considerable progress has been made towards understanding the mechanisms of these reactions; however, there are certain aspects which still require clarification. The recent development of syntheses[2] of "ligand free"[3] zerovalent compounds of platinum now allows a study of reactions of these species with 1,3-dienes. Herein we report studies with bis(cycloocta-1,5-diene)platinum.[4]

Reaction (room temperature, 1 h) of an excess of 2,3-dimethylbuta-1,3-diene with bis(cycloocta-1,5-diene)platinum afforded (84% yield) the white crystalline complex I,[5] mp 95° dec [^{13}C NMR resonances (C_6D_6, ^{1}H decoupled, measured downfield from Me_4Si) at 20.1 ppm, C(3) ($J_{PtC(3)}$ = 111.4 Hz); 40.7, C(1) ($J_{PtC(1)}$ = 787.4 Hz); and 136.4, C(2) ($J_{PtC(2)}$ = 0Hz); resonances due to coordinated C_8H_{12} occur at 29.6 and 96.8 ppm (J_{PtC} = 51.9 Hz)]. Treatment of I with *tert*-butylisocyanide led to the displacement of cycloocta-1,5-diene and the formation of II, mp 84–86° [^{13}C NMR resonances (C_6D_6, ^{1}H decoupled) at 21.4 ppm, C(3) ($J_{PtC(3)}$ = 96.1 Hz); 30.9, C(1) ($J_{PtC(1)}$ = 608.8 Hz); and 136.2, C(2) ($J_{PtC(2)}$ = 46.2 Hz); together with resonances due to coordinated *t*-BuNC]. Thus, the reaction involves an oxidative 1,4-addition of a Pt(0) species to the 1,3-diene to form a platinacyclopent-3-ene. Although this mode of metal–diene interaction has been observed previously with Ni(0) complexes[6] and the perfluorinated diene CF_2:CFCF:CF_2, this is the first example of such a reaction with a hydrocarbon.[7]



(I, L_2 = 1,5-C_8H_{12})
(II, L = *t*-BuNC)



(III, L_2 = 1,5-C_8H_{12})
(IV, L = *t*-BuNC)

It is likely that the reaction involves the intermediacy of (cycloocta - 1,5 - diene)(2,3-dimethylbuta-1,3-diene)-platinum(0), which undergoes an electronic rearrangement to form the Pt(II) five-membered ring species. There has been considerable discussion about the possibility that bisolefin complexes could reversibly transform into a metallocyclopentane.[8]

In contrast, buta-1,3-diene reacts (room temperature, 2 h) with [Pt(1,5-C_8H_{12})$_2$] to form complex III, mp 110 °C. Examination of the ^{1}H and ^{13}C NMR spectra showed that III was a 2,5-divinylplatinacyclopentane; however, the important question as to the relative configuration of the vinyl groups remained undefined. A single-crystal x-ray diffraction study established the structure shown in Figure 1. Crystal data: $C_{16}H_{24}Pt$; monoclinic; $P2_1/n$; Z = 4 in a unit cell of dimensions a = 9.082 (6), b = 10.554 (13), c = 15.293 (4) Å; β = 92.13 (7)°; R is currently 0.12 for 1487 reflections with $I \geq 2.0\sigma(I)$ (Syntex $P2_1$ four-circle diffractometer using Mo K_α radiation). The crystal of III was twinned and the resulting structure showed disorder; therefore, further structural confirmation was sought. Cycloocta-1,5-diene was displaced from III by *tert*-butyl isocyanide to give complex IV, mp 111–112°, whose crystal structure was also determined (Figure 2). Crystal data: $C_{18}H_{30}N_2Pt$; monoclinic; $P2_1/n$; Z = 4 in a unit cell of dimensions, a = 9.317 (4), b = 12.284 (12), c = 19.217 (15) Å; β = 99.16(5)°; R is currently 0.10 for 1100 reflections with $I \geq 2.0\sigma(I)$.

Despite the problems of crystal imperfection the structures of both III and IV showed unequivocally that the vinyl groups lie on opposite sides of the five-membered ring with deviations of 0.84 and −0.97 Å in III and −0.64 and 0.71 Å in IV, respectively, from the mean coordination plane. An insight into the mode of formation of the *trans*-2,5-divinylplatinacyclopentane ring system was obtained from a study of the reaction of bis(ethylene)trimethylphosphineplatinum with buta-1,3-