

Figure 2. CPMAS/DD ¹³C NMR spectra of crystalline s-TPH (b) and s-TPN (a) recorded at room temperature at 50.3 MHz on a Varian XL-200 spectrometer equipped with a Doty Scientific solids probe. Both samples were spun at the magic angle at a speed of ca. 2.5 kHz; a 40 kHz rf field strength was applied for 200 ms to achieve ¹H dipolar decoupling; and a 2.5-ms cross-polarization contact time was employed. Both spectra were referenced to external poly(oxymethylene) which resonates¹⁵ at 89.1 ppm from TMS. Resonances marked with an X are the spinning sidebands of the aromatic carbon resonances. Expansions of the CH₂ and CH region of the s-TPN and s-TPH spectra are shown in parts c and d, while expansions of the C¹ region are shown in parts e and f.

observed in solid-state polymer ¹³C NMR spectra to their solidstate conformations, we expect the pattern of ¹³C resonances summarized in Table I. The central (C) methylene carbons in s-TPN and the methylene carbons in s-TPH should resonate downfield from the terminal (T) methylenes in s-TPN, because the T CH₂'s (s-TPN) are shielded by the gauche arrangement of their γ -substituents [CH(C)'s] (see Figure 1), while the central CH₂'s in s-TPN and the s-TPH methylenes are trans to their γ -CH(T)'s and are not shielded. The difference in methylene carbon chemical shifts should be ca. 5 ppm (γ_{CH_2CH}), judging from previous experience.^{13,14}

The methylene carbons in all-trans, planar-zigzag form I s-PS are not shielded by their γ -CH's, and they resonate at 48.4 ppm¹⁰ very near the central CH₂'s in s-TPN and the s-TPH methylenes.

The four quaternary, aromatic carbons of s-TPN [C¹(C) and C¹(T)] and the two terminal quaternary, aromatic carbons of s-TPH [C¹(T)] should resonate downfield from the central C¹ in s-TPH, because C¹(C) in s-TPH is shielded by two $\gamma_{C^1,CH}$, while the other C¹ carbons possess only a single $\gamma_{C^1,CH}$ interaction (see Figure 1). This additional shielding ($\gamma_{C^1,CH}$) should^{13,14} move $\delta(C^1(C))$ in s-TPH ca. 2.5 ppm upfield from the remaining quaternary carbons in both s-PS model compounds.

The CPMAS/DD ¹³C NMR spectra of crystalline s-TPH and s-TPN are presented in Figure 2. It is clear from their comparison¹⁶ that the methylene and quaternary, aromatic carbon chemical shifts follow the pattern expected (Table I) from consideration of their crystalline conformations in terms of γ -gauche shielding effects. As a consequence, our previous analysis¹⁰ of the ¹³C chemical shifts observed in the high-resolution, solid-state ¹³C NMR spectra of forms I and II s-PS is confirmed, and the conclusion that forms I and II s-PS adopt the ...*tttttttt...* and ...*ttggttgg...* conformations, respectively, receives further support.

Palladium-Catalyzed Carboannulation of 1,3-Dienes by Aryl Halides

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Carboannulation processes are among the most important reactions in organic synthesis, but few have proven very general in scope.^{1,2} The addition of arylpalladium species to 1,3-dienes is known to afford π -allylpalladium compounds,³ and extensive work

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In form II s-PS the methylene carbons resonate at 49.1 and 38.1 ppm reflecting 0 and 2 gauche shielding arrangements with their γ -CH's, respectively, in the ...*ttggttgg*... conformation proposed for this s-PS polymorph. The terminal CH₂ carbons in s-TPN resonate at 43.5 ppm (see Figure 2), or midway between the CH₂ carbons in form II s-PS, because these T CH₂'s are gauche to a single γ -substituent, CH(C).

⁽¹⁶⁾ Note the doubling of most resonances in the CPMAS/DD ¹³C NMR spectrum of s-TPH shown in Figure 2b. This most likely reflects the fact that two s-TPH molecules form the asymmetric unit of its crystalline unit cell, and each experiences different intermolecular packing interactions. A single s-TPN molecule constitutes the asymmetric unit in its crystalline unit cell, and as expected we observe only single resonances for each carbon type (see Figure 2a).

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| Table I. | Palladium-Catalyze | d Carboannulation | of | 1.3-Dienes ^a |
|----------|---------------------|-------------------|-----|-------------------------|
| 1401010 | I allugium Calarine | | ••• | ., |

| entry | aryl halide | 1,3-diene | base | PPh ₃ | reactn conditns | product ⁶ | % isolated yield |
|-------------|--|--|---------------------------------|------------------|--|---|--|
| 1 | | <i>n</i> -C ₄ H ₉ CH=CHCH=CH ₂ | Na ₂ CO ₃ | + | 60 °C, 1 day | | 87 |
| 2 | | (Z)-CH ₃ CH=CHCH=CH ₂ | Na ₂ CO ₃ | + | 60 °C, 2 days | CO ₂ Et CO ₂ Et | 95° |
| 3 | | сн _а н ₂ с=ссн=сн ₂ | Na ₂ CO ₃ | + | 60 °C, 12 days | CO ₂ Et CO ₂ Et | 92 |
| 4 | | н₃с сн₃ н₂с≕с—с≕сн₂ | Na ₂ CO ₃ | + | 60 °C, 17 days | | 84 |
| | CH ₂ CH ₂ CHXCO ₂ R | \bigcirc | | | | CO ₂ R H ¹¹ | |
| 5 6 7 | | | NaOAc Na2CO3 NaOAc | - + - | 80 °C, 1 day 80 °C, 3 days 80 °C, 4 days | $\begin{array}{c c} R & X \\ \hline Et & CO_2Et \\ Et & CN \\ Me & SPh \end{array}$ | 85 73 ^{d.e} 96 ^e |
| 8 | $\operatorname{CH}(\operatorname{CO}_2\operatorname{Et})_2$ | СН ₃ H ₂ C == CHC==CH ₂ | Na ₂ CO ₃ | + | 60 °C, 8 days | | 82 |
| 9 | | \bigcirc | Na ₂ CO ₃ | + | 60 °C, 10 days | EtO ₂ C CO ₂ Et | 86 |
| 10 | $\operatorname{CH}_{\mathrm{I}}^{\mathrm{CH}(\mathrm{CO}_{2}\mathrm{Me})_{2}}$ | \bigcirc | Na ₂ CO ₃ | - | 60 °C, 1 day | MeO ₂ C CO ₂ Me | 87 |
| 11 | CH ₂ CO ₂ Et | \bigcirc | KOAc | | 80 °C, 2 days | | 85* |
| 12 | | \bigcirc | KOAc | + | 80 °C, 1 day | | 56 |
| 13 | CH ₂ CH ₂ CH ₂ NO ₂ | \bigcirc | Li ₂ CO ₃ | + | 80 °C, 7 days | | 73 |

All reactions were run by heating 5% palladium acetate, 1 equiv of aryl iodide, 5 equiv of 1,3-diene, 1 equiv of n-Bu4NCl, 5 equiv of base, DMF (4 mL/mmol of aryl halide) and where appropriate 5% of PPh₃ or P(OPh)₃. ^bAll products gave appropriate ¹H and ¹³C NMR, IR, and mass spectral or elemental analysis data. ^cE:Z ratio is 8:1. ^d Eleven percent of o-IC₆H₄CH₂CH₂CN was also formed. ^cA mixture of diastereomers about the ester group is present.

on the inter- and intramolecular displacement of palladium from π -allylpalladium compounds by carbon nucleophiles has also been reported.⁴ We report that the coupling of these two processes affords a convenient, versatile, new route for the carboannulation of 1,3-dienes as indicated by the examples reported in Table I.

Best results have been obtained by using 5% Pd(OAc)₂, 1 equiv of *n*-Bu₄NCl, and carbonate or acetate bases in DMF at 60-80 °C.^{5.6} While catalytic amounts of PPh₃ are not necessary, the yield, regioselectivity, and amount of 1-aryl 1,3-diene side product are frequently improved by its presence.

Unlike intermolecular π -allylpalladium carbanion displacement processes, which usually require carbanions stabilized by at least two strong electron-withdrawing groups,⁷ our intramolecular

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displacement process is quite successful when a single such group is present (entries 11-13). The ability to generate in a single step highly functionalized carbocycles amenable to further functional-group manipulation, such as that shown in eq 1, is one of the most important features of this process.



A wide variety of 1,3-dienes undergo facile, regioselective carboannulation. While we have generally employed 5 equiv of the readily available diene, only slightly reduced yields of carbocycle are obtained when 2 or even 1 equiv of diene is used (Table I, entry 5: 5 equiv, 85%; 2 equiv, 77%; 1 equiv, 76%), but the reaction time is increased substantially (1 day, 6 days, and 7 days, respectively). Simple linear trans-dienes afford exclusively the trans olefinic product, but cis-1,3-pentadiene affords approximately an 8:1 ratio of E:Z olefinic products (entry 2).

This carboannulation process most likely proceeds by (1) reduction of $Pd(OAc)_2$ to the actual catalyst Pd(0), (2) oxidative addition of the aryl halide to Pd(0), (3) arylpalladation of the 1,3-diene to form a π -allylpalladium intermediate, and (4) formation of the neighboring carbanion and subsequent front- or backside displacement of palladium, which regenerates the Pd(0)catalyst. The predominant formation of the trans product from cis-1,3-pentadiene (entry 2) is best explained by isomerization of an initially formed anti π -allylpalladium intermediate to the more thermodynamically stable syn intermediate.¹⁰ The presence of some cis product, however, suggests that palladium displacement either can occur through a σ -allylpalladium intermediate or is sufficiently rapid to occur via the initially formed anti π -allylpalladium intermediate prior to isomerization. Since all fivemembered-ring products contain exclusively cis ring fusion as determined by ¹H NMR spectroscopy,¹¹ they are most likely arising by halide displacement from the initially formed π -allylpalladium intermediate by the tethered nucleophile and subsequent reductive elimination with retention, an unusual path for palladium displacement by stabilized carbanions.⁴ All six-membered-ring products contain exclusively a trans ring fusion as determined by ¹H NMR spectroscopy,¹² most likely formed by backside palladium displacement.

In conclusion, the simple palladium-catalyzed arylannulation of 1,3-dienes by functionally substituted aryl halides utilizes readily available starting materials and proceeds under mild conditions in high yield, completely stereo- and regioselectively, to form a wide variety of functionally substituted carbocycles.

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Supplementary Material Available: General procedure for carboannulation reactions and experimental data (NMR, IR, elemental analysis) for 1-13 (6 pages). Ordering information is given on any current masthead page.

Stereochemical Studies of Coenzyme F430 Based on **2D NOESY Back-Calculations**

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Coenzyme F430 is a nickel-containing tetrapyrrole from methanogenic bacteria that is utilized in the biocatalytic conversion of CO_2 to methane.¹⁻⁶ Although atomic-level structural data for F430 are lacking, elegant one-dimensional (1D) NMR experiments have led to the primary structure determination of the pentamethyl ester derivative (F430M), and 1D nuclear Overhauser effect (NOE) data in combination with chemical data provided a partial stereochemical assignment for the F430M corphin macrocycle.7-10 The stereochemistry of the C17 carbon (Figure 1) could not be assigned due to severe signal overlap, and the relative stereochemical assignments for C18 and C19 were assigned on the basis of weaker NMR and chemical data and might be considered tentative.^{8,11} The C17-C18-C19 stereochemical assignments were determined recently by 2D NMR to be either R, R, S (consistent with the original stereochemical assignments) or S,S,R (reverse assignment).¹² We describe here the results of a new approach for stereochemical analysis that employs 2D NOESY back-calculations for F430 model structures generated by distance geometry (DG) computations.

DG calculations were performed with DSPACE.¹³⁻¹⁶ Covalency constraints dictated by the primary structures of the original and

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⁽¹²⁾ Six-membered-ring products, such as the product reported in entry 13 in Table I, which exhibits J = 11.7 Hz coupling between the two hydrogens on the ring-fused carbons, exhibit coupling constants only consistent with an axial-axial arrangement of the two hydrogens.

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