Table I. Calculated Methyl Stabilization Energies, $CH_4 + XCH_2Y \rightarrow CH_3X + CH_3Y$, in kcal/mol $(3\text{-}21G(*)//3\text{-}21G(*))^a$ for XCH_2Y Species in Their Most Stable Conformations

X	Y					
	NH₂	OH	F	PH₂	SH	Cl
NH₂	10.6 (12.2)	12.7 (11.5)	17.6	0.8	4.2	10.5
OH		17.4 (15.7)[b]	16.2	0.5	4.7	5.8
F			13.9 (12.9)[c]	0.2	1.8	1.1
PH2				0.5	0.4	−0.2
SH					0.1	−1.3
Cl						−4.3 (−3.7)[d]

[a] This basis includes d functions only on second-row atoms; the 3-21G basis is employed for the other atoms. Much of the data for reference compounds were taken from: "Carnegie-Mellon Quantum Chemistry Archive", 3rd ed.; Whiteside, R. A., Frisch, M. J., Pople, J. A., Eds.; Carnegie-Mellon University, 1983. Values in parentheses, taken from this source, are at $6\text{-}31G*//6\text{-}31G*$. This basis has d functions on all non-hydrogen atoms. Also see ref 4 and 10. [b] Exptl: 15 ± 1.5 kcal/mol.[7] [c] Exptl: 12 ± 4.1 kcal/mol.[7] [d] The MP2/6-31G*//6-31G* value is −0.3 kcal/mol. exptl: 1.5 ± 1.4 kcal/mol.[7]

SH, and PH₂ (Table I, lower entries). This can be attributed to the combination of the inherently low π-donor ability of these groups and to the lower electronegativity of the elements of the second row relative to their first-row counterparts. Such groups are relatively poor π-donors and poor σ-acceptors. Even H₂PCH₂Cl, which combines a second-row lone pair group (PH₂) with the most electronegative second-row atom (Cl), shows a very small effect. While the favored conformation of this molecule (1) has the phosphorus lone pair and the C–Cl bond in a trans-parallel orientation, the other staggered conformation is only 1.1 kcal/mol higher in energy. Second-row molecules like PH₃ and SH₂ have smaller bond angles than their first-row counterparts, e.g., NH₃ and OH₂. This bending also decreases the π-donor abilities of the lone pair orbitals on second-row groups.

The last category of XCH₂Y molecules (Table I, upper right) represents combinations of first-row substituents, X, with second-row groups, Y. Even here, some of the stabilization energies are negligibly small. This is true for all compounds involving PH₂ (XCH₂PH₂) and all compounds involving fluorine (FCH₂Y). This shows that the second-row groups are ineffective as π-donors.

However, there are significant anomeric interactions involving second-row substituents. The best combination, ClCH₂NH₂, has a methyl stabilization energy of 10.5 kcal/mol due to the relatively high electronegativity (σ-withdrawing ability) of chlorine and the good π-donating ability of NH₂. This also results in a preference for the trans lone pair–halogen conformation 1. A smaller methyl stabilization energy, 4.2 kcal/mol, is found in NH₂CH₂SH which again favors a similar geometry. The SH group is best oriented as shown in 2, but the energetic preference is not large. An appreciable stabilization energy of 5.8 kcal/mol is found in HOCH₂Cl (3); this is a model for the many α-chlorinated ethers which have been observed experimentally to prefer gauche conformations.[4,10] The other conformations are several kcal/mol higher in energy. The final example, HOCH₂SH, mirrors the behavior of CH₂(OH)₂ which has been extensively investigated.[8,9] However, the stabilization energy of the sulfur system, 4.7 kcal/mol, is very much less than that of HOCH₂OH, 17.4 kcal/mol. The same gauche-(+) conformation 4 is prefered in the sulfur compound as in the oxygen case, but the magnitude of the energy differences between the various alternative conformations is considerably less.

The NH₂ π-donor, Cl σ-acceptor character of the interaction was demonstrated by model 6-31G* calculations on NH₂CH₂Cl geometries in which the NH₂ groups were held planar and C_s symmetries imposed. The methyl stabilization energy (9.7 kcal/mol vs. CH₃NH₂ with a planar NH₂ group) of the conformation like 1 was reduced to 2.5 kcal/mol by a 90° NH₂ rotation which "shut off" the N π-donor effect. This rotation decreased the C–Cl bond length by 0.07 Å. The results for FCH₂NH₂ (planar NH₂) were similar (reduction of the methyl stabilization energy from 15.8 to 8.0 kcal/mol by 90° NH₂ rotation). The residual stabilization was due to the F π-donor, NH₂ σ-acceptor interaction.

In conclusion, anomeric effects involving second-row substituents are greatly attenuated relative to their first-row counterparts. This can be attributed to the poorer π-donating and the lower elec-

tronegativity of the second-row groups. The other effects that normally control stereochemistry may thus predominate. If these results are extrapolated to groups involving elements of the lower rows in the periodic table, anomeric effects should tend to vanish. Residual interactions may be expected only in systems like NH₂CH₂Br.

The absolute energies and full description of the geometries of all new systems calculated in this paper are available in the supplementary material. The full report, to be published subsequently, will contain additional data at higher levels of theory, but the general conclusions drawn in this paper are not expected to be altered significantly.

Supplementary Material Available: Full listings of the absolute energies and geometries of all CH₂XY species calculated in this work (5 pages). Ordering information is given on any current masthead page.
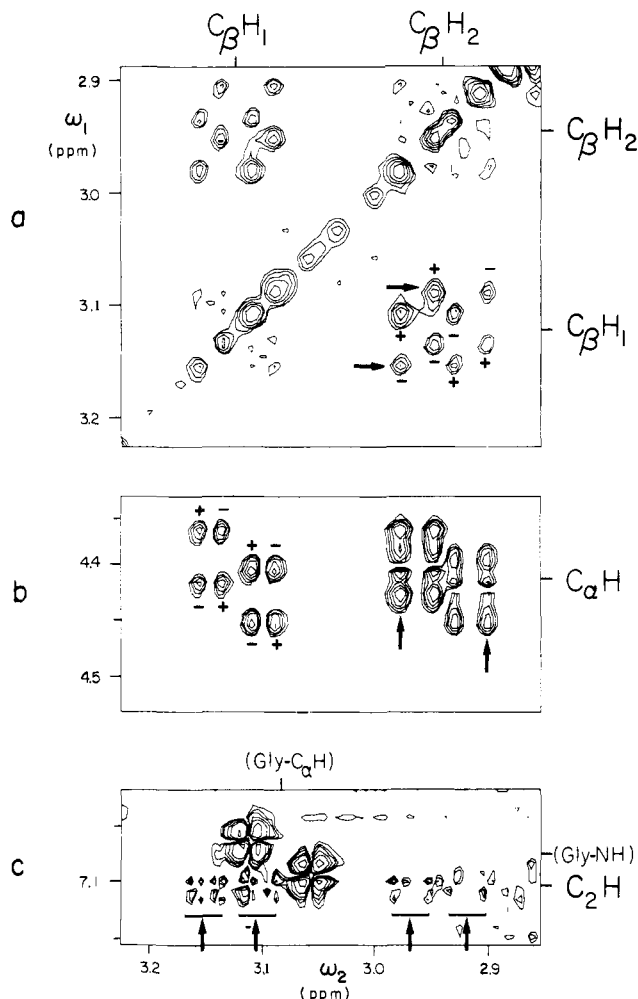
Two-Dimensional Correlation of Connected NMR Transitions

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Two-dimensional (2D) NMR correlation spectroscopy[1-5] (COSY) has been established as a powerful method for the elucidation of proton–proton scalar coupling networks. The most attractive variant so far combines multiple-quantum (MQ) filtering[6,7] with phase-sensitive data display[8] to yield a 2D spectrum
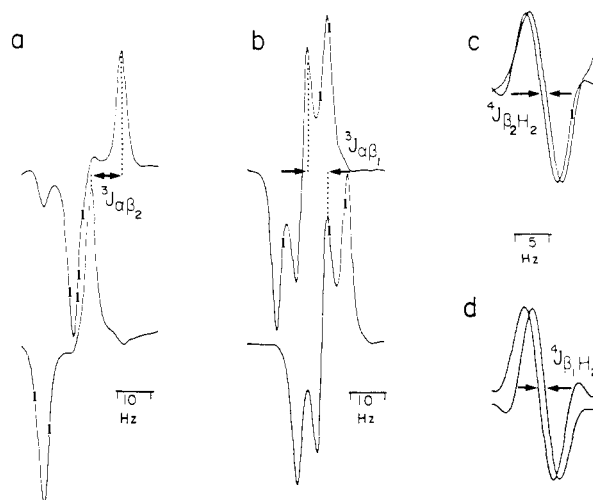
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Figure 2. Pairs of sections cut through cross-peak multiplets in Figure 1 at the positions of the arrows. Half of the traces have been phase-inverted to ease comparison. Traces (a) (from figure 1a) yield $J_{\alpha\beta_2} = 8.6$ Hz. Traces (b) (from the $C_\beta H_2$-$C_\alpha H$ cross-peak symmetrical with respect to the arrows in Figure 1b) yield $J_{\alpha\beta_1} = 5.7$ Hz. The traces (c) ($J_{\beta_2 H_2} = -0.6$ Hz) and (d) ($J_{\beta_1 H_2} = -1.0$ Hz) were obtained by integration over the parts of the cross-peaks marked by brackets in Figure 1c to improve sensitivity.

Figure 1. Details from the 300-MHz E. COSY spectrum of *cyclo*-(Pro-Phe-D-Trp-Lys(Z)-Thr-Gly) in Me_2SO-d_6 showing diagonal peaks and cross-peaks involving the C_β protons of tryptophan. Contours are drawn for positive and negative intensities. The following relative signs of coupling constants can be determined: The two $^3J_{\alpha\beta}$ couplings have signs opposite to that of $^2J_{\beta_1\beta_2}$. The four-bond couplings have the same sign as $^2J_{\beta_1\beta_2}$ (less obvious because the ^4J couplings are small, compare Figure 2). Note that the C_2H-$C_\beta H_1$ cross-peak in the corresponding 2Q-filtered COSY spectrum would have been almost completely covered by the neighboring more intense NH-$C_\alpha H$ cross-peak of the Gly residue. All nonvanishing multiplet components in this spectrum have the same intensity as they would have in a 2Q-filtered COSY spectrum for the same measuring time.[12]

with high resolution[9] due to the pure absorption line shapes. The achieved resolution often allows the accurate measurement of all coupling constants from a single COSY spectrum in systems of limited complexity. For larger spin systems, however, the determination of J coupling constants from COSY spectra is often impeded by the overlap of numerous multiplet components.

The assignment and measurement of J coupling constants would be facilitated by the restriction of coherence transfer to transitions directly connected in the energy level diagram, i.e., transitions possessing a common energy level. No information would be lost and the simplified cross-peak multiplet patterns would make coupling information more accessible. A system of N mutually coupled protons leads to cross-peaks with 2^{2N-2} multiplet components in conventional COSY, while only 2^N represent correlations between connected transitions. Several approaches toward restricting the coherence transfer have been proposed,[1,4,5,10,11] but

they suffered either from mixed line shapes or form an unfavorable ratio of cross- to diagonal-peak intensities.

In this paper, we present a 2D correlation technique where coherence transfer takes place exlusively between connected transitions as long as the spins are weakly coupled. We call the technique "exclusive correlation spectroscopy" (E. COSY). A detailed account of the technique is given at another place.[12] It suffices to recognize that the coherence transfer between connected transitions and between nonconnected transitions have different dependencies on the rotation angle β of the mixing pulse. This fact can be exploited for eliminating multiplet components corresponding to correlations between nonconnected transitions by combining experiments with different rotation angle β.

Instead of using a variable rotation angle β in the sequence $(\pi/2)_x$-t_1-$(\beta)_y$-t_2, it is more accurate to employ the equivalent sequence $(\pi/2)_\beta$-t_1-$(\pi/2)_\beta(\pi/2)_{-x}$-$t_2$ where the variable parameter β appears as a phase shift. This is the basic experiment used for MQ filtering, and the proposed experiment may be understood as a combination of MQ-filtered COSY spectra of different orders.[13] The highest order to be used in the combination depends on the coupling networks. A p-quantum-filtered (pQ-filtered) spectrum must be included only if a pair of coupled spins is expected with at least $p - 2$ common coupling partners.[6] In practice, it is often sufficient to combine pQ-filtered spectra for $p = 2, 3$, and 4 (in the ratio 1:2:4).[13]

We demonstrate the features of this novel technique by determining signs and magnitudes of J coupling constants in the tryptophan residue of the cyclic hexapeptide *cyclo*-(Pro-Phe-D-Trp-Lys(Z)-Thr-Gly) in its dominant conformation. For the E. COSY cross-peaks resulting from the coupling network limited by the NH proton in the peptide bond and the indole NH, it is sufficient to combine 2Q- and 3Q-filtered spectra. Optimum sensitivity for the E. COSY experiment s(E. COSY) is achieved by the following linear combination of phase-shifted experiments $s(\beta)$: s(E. COSY) $= 4s(\beta = 0°) - 3s(60°) + s(120°) + s(240°) - 3s(300°)$, the factors indicating the number of experiments performed for each β value.

Figure 1 shows excerpts from the E. COSY spectrum involving the C_β protons. Each cross-peak multiplet contains quadratic

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four-line patterns with the signs ($^{+}_{-}{}^{-}_{+}$) due to the coupling between the active spins A$_1$ and A$_2$, as indicated in Figure 1.[14]   Each passive spin P splits the basic four-peak pattern into two identical patterns which are displaced by the coupling constants J_{PA_1} in the ω_1- and J_{PA_2} in the ω_2-dimension or vice versa. Even if one of these coupling constants, e.g., J_{PA_2}, in the ω_2-dimension, is smaller than the line width, it can still be determined by comparing two traces parallel to the ω_2-axis cut through multiplet peaks separated from the rest of the multiplet by $2\pi J_{PA_1}$ in the ω_1-dimension (indicated by arrows in Figure 1). Examples are shown in Figure 2.   The shift of the (identical) multiplets in the pair of traces indicates the desired passive coupling constant. The couplings $^3J_{\alpha\beta_1}$ and $^3J_{\alpha\beta_2}$ determined from Figure 2a,b are sufficiently resolved to be already visible in the 2D spectrum of Figure 1. However, the two couplings $^4J_{\beta_1 H_2}$ and $^4J_{\beta_2 H_2}$ do not lead to a resolved structure in the 2D spectrum. $^4J_{\beta_2 H_2}$, for example, can be determined from the C$_2$H–C$_\beta$H$_1$ cross-peak by the relative shift induced parallel to the ω_1-axis of the traces obtained by integration over the multiplet patterns (marked by brackets) which are displaced in the ω_2-dimension by the coupling $2\pi^2 J_{\beta_1\beta_2}$ (Figure 2c). In the same manner, $^4J_{\beta_1 H_2}$ can be measured from the cross-peak C$_2$H–C$_\beta$H$_2$ (Figure 2d).

The proposed E. COSY experiment appears powerful for the determination of magnitude and signs of coupling constants in complex spin systems. Furthermore, the E. COSY procedure favors the diagonal peaks (at $\omega_1 = \omega_2$) in the diagonal multiplets (see Figure 1a). This allows the analysis of cross-peak multiplets even closer to the diagonal than for 2Q-filtered COSY spectra. Finally, the basic principle of E. COSY is not limited to the experiment discussed but can also be applied in connection with multiple quantum spectroscopy and for the simplification of cross-peak multiplets in NOESY spectra.

(14) In some cases, passive couplings cause square patterns to partially overlap leading to rectangular patterns due to annihilation of peaks of opposite sign (see Figure 1b).

Palladium-Promoted Diels–Alder Cycloadditions to 1-Phenyl-3,4-dimethylphosphole. Facile Synthesis of a New Class of Rigid Chiral Bidentate Phosphines: 5-Phosphino-7-phosphabicyclo[2.2.1]hept-2-enes

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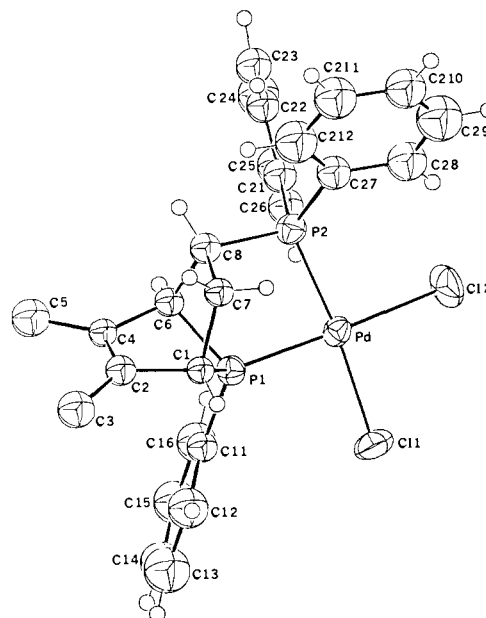*Reno, Nevada 89557*

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We have previously investigated[1] the synthesis of mixed-ligand palladium complexes of the type LL'PdX$_2$, palladium complexes of phospholes,[2] and reviewed the coordination chemistry of phospholes.[3]   From these previous studies we noted that (1) the

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Figure 1. Structure of dichloro[5-(diphenylphosphino)-2,3-dimethyl-7-phenylphosphabicyclo[2.2.1]hept-2-ene]palladium(II) showing the 50% probability ellipsoids. Selected bond distances (Å): PdP$_1$, 2.213 (4); PdP$_2$, 2.251 (4); PdCl$_1$, 2.344 (4); PdCl$_2$, 2.351 (4); P$_2$C$_8$, 1.868 (13); P$_1$C$_1$, 1.818 (13); P$_1$C$_6$, 1.823 (14). Selected bond angles (deg): P$_1$PdP$_2$, 83.5 (1); Cl$_1$PdCl$_2$, 92.6 (2); Cl$_1$PdP$_1$, 89.2 (1); Cl$_2$PdP$_1$, 173.6 (1); Cl$_1$PdP$_2$, 171.4 (1); C$_1$P$_1$C$_6$, 82.5 (6). The molecule of CH$_2$Cl$_2$ was located and refined.

mixed-ligand complexes were rapidly formed in solution according to reaction 1, (2) the mixed-ligand complexes generally possessed

$$L_2PdX_2 + L'_2PdX_2 \rightleftharpoons 2LL'PdX_2 \qquad (1)$$
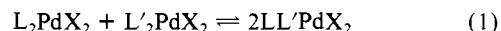
the cis geometry, (3) coordination of a phosphole polarizes its double bonds resulting in increased electron density at the α-carbon centers, and (4) coordination of a phosphole increases its propensity to undergo [4 + 2]-Diels–Alder cycloadditions with dienophiles. Thus, we reasoned that reaction of a palladium phosphole complex with a palladium vinylphosphine complex should likewise produce the *cis*-(phosphole)(vinylphosphine)palladium complex which might then undergo an internal Diels–Alder-[4 + 2] cycloaddition to yield a new class of chiral diphosphines, the 5-phosphino-7-phosphabicyclo[2.2.1]hept-2-enes according to reaction 2.
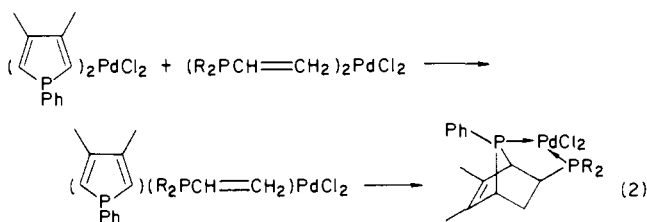
Accordingly, when a solution containing dichlorobis(1-phenyl-3,4-dimethylphosphole)palladium(II) ($\delta(^{31}P)$ 26.4) was added to a solution containing an equal molar amount of dichlorobis(diphenylvinylphosphine)palladium(II) ($\delta(^{31}P)$ 19.4, cis isomer; 11.2, trans isomer; 40:60, respectively) in CH$_2$Cl$_2$ at ambient temperature an AX^{31}P NMR spectrum ($\delta(^{31}P)$ 124.0, 34.5, J_{PP} = 5 Hz) was immediately observed. The low-field resonance (124.0 ppm) is typical[4] of phosphorus contained in a 7-phosphabicyclo[2.2.1]hept-2-ene. This ^{31}P NMR spectrum suggested that reaction 2 proceeded to completion and that none

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