

¹³C, ¹⁵N, and ³¹P NMR Spectroscopic Studies of *N*-Aroyl-*P,P,P*-triphenylphospha-λ⁵-azenes

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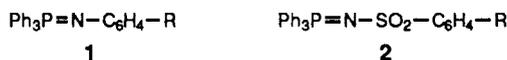
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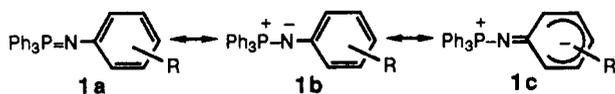
The ¹³C, ¹⁵N, and ³¹P NMR spectra of a series of *N*-aroyl-*P,P,P*-triphenylphospha-λ⁵-azenes **3** are reported. The syntheses of several heretofore unknown members of this class of compounds are also reported along with the syntheses of ¹⁵N-labeled compounds. The parent substituted benzamides **4**, including ¹⁵N-labeled derivatives, have also been examined by ¹³C and ¹⁵N NMR spectroscopy. Correlation of the ³¹P, ¹⁵N, and various ¹³C chemical shifts with Hammett substituent constants suggests that **3** can be viewed as being made up of three interacting dipolar subunits as shown in Figure 1. This is based on the slope of the plots of the chemical shifts for various atoms vs the Hammett constants. The response of the one-bond coupling constants ¹J_{PN} and ¹J_{PC} to changes in substituent is consistent with pπ-dπ and pπ-σ* (using a P-C σ* orbital) between the P and N atoms. Alternatively, one can explain the changes in ¹J_{PN}, ¹J_{PC} and also ¹J_{NC} on the basis of electrostatic interactions based on the structure in Figure 1, by assuming that adjacent atoms with opposite charge will attract, shorten the bond, increase the s character of the orbitals making up the bond, and thus increase the one-bond coupling constant. The opposite will be true for atoms that repel one another. The ¹³C and ¹⁵N chemical shifts in **3** correlate with those in **4**. From the sign of the slopes of these correlations, one can show that the positively charged phosphorus atom of the phosphazanyl group polarizes the rest of the molecule (N, CO, and aryl group) relative to the benzamides. The ipso carbon atoms in *N*-aryl-*P,P,P*-triphenylphospha-λ⁵-azenes **1**, *N*-(arylsulfonyl)-*P,P,P*-triphenylphospha-λ⁵-azenes **2**, **3**, **4**, the anilines **5**, and arenesulfonamides **6** have all been compared by treatment with the Taft DSP and the DSP-NLR equations. The conclusions are that the Ph₃P=N group is a strongly electron donating group and is even more electron donating than NH₂. The Ph₃P=NSO₂ group is moderately electron withdrawing while the H₂NSO₂ group is much more strongly electron withdrawing. Ph₃P=NC(O) and H₂NC(O) both appear to be about equally moderately electron withdrawing with the former group (in **3**) being a little less electron withdrawing. This small difference between these groups may be the result of the ability of the nitrogen to interact more strongly with the aromatic ring by back donation.

Introduction

Our interest in the synthesis and properties of phosphazene systems has afforded us the opportunity to study the multinuclear NMR spectroscopy of these compounds.²⁻⁴ In particular we have examined and reported on the ³¹P, ¹⁵N, and ¹³C NMR spectra of a series of *N*-aryl-*P,P,P*-triphenylphospha-λ⁵-azenes **1** and *N*-(arylsulfonyl)-*P,P,P*-triphenylphospha-λ⁵-azenes **2**. Based



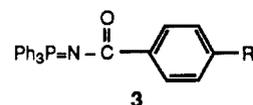
upon the effect of the substituents in **1** on the ³¹P, ¹⁵N, and ¹³C chemical shifts, we found considerable charge delocalization into the aryl ring, as shown in structures **1a-c**.



Indeed the use of substituents such as *p*-NO₂ and *p*-CN, where direct resonance interaction of this group with the electron pair is possible, provided Hammett correlations with σ⁻ rather than with σ. The change in the relative contributions of the resonance forms **1a-c** also changed the coupling constants, ¹J_{PN} and ¹J_{PC}, and it was suggested that this was due to changes in the extent of phosphorus-nitrogen double bonding. Quantum mechanical PRDDO calculations showed that this PN double bond is most likely composed of both pπ-dπ and pπ-σ* compo-

nents, where the latter involves the P-C (phenyl) bond.³ When the resonance insulating but inductively transmitting SO₂ group was put between the nitrogen and the aryl ring, the substituent chemical shift effect diminished somewhat on the P, N, and ¹³C atoms in the *P*-phenyl rings and now the ³¹P and ¹³C chemical shifts showed Hammett correlations with σ rather than σ⁻. Again changes in the coupling constants ¹J_{PN} and ¹J_{PC} were consistent with σ and π bonding effects including both pπ-dπ and pπ-σ* multiple PN bonding.

In this paper we report on the multinuclear NMR study (³¹P, ¹⁵N, and ¹³C) of a series of compounds, *N*-aroyl-*P,P,P*-triphenylphospha-λ⁵-azenes **3**, where now a carbonyl



- | | | |
|-------------------------|-----------|------------------------|
| a: R = NMe ₂ | e: R = Me | i: R = Br |
| b: R = <i>O-n</i> Bu | f: R = H | j: R = CN |
| c: R = OMe | g: R = F | k: R = NO ₂ |
| d: R = Et | h: R = Cl | |

has been put between the nitrogen and the substituted aryl ring. The resonance forms shown below, A-F, are now possible (with E no doubt contributing less than the others) and so there can be direct resonance between the substituent and the carbonyl and between the nitrogen and the carbonyl. Because of the cross conjugation of the carbonyl with the nitrogen and the aromatic ring, one can not write an uncharged canonical form involving direct resonance interaction between the nitrogen and the aromatic ring. However, there must be an interaction through the carbonyl group both via an inductive effect and by way of resonance forms C and E.

Syntheses

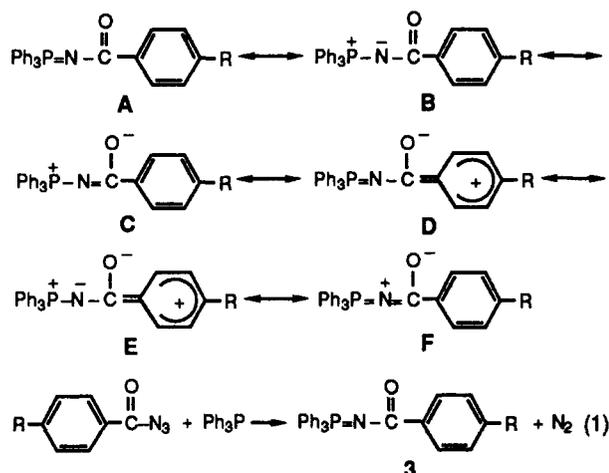
The syntheses of **3c,e-k** are given in ref 5. Compounds **3a,b,d** were prepared from the aroyl azide and triphenylphosphine (eq 1).⁵ The ¹⁵N-labeled compounds

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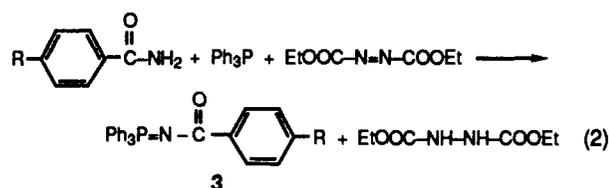
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were all prepared from either ^{15}N -labeled benzamides with triphenylphosphine and diethyl azodicarboxylate (eq 2)^{5,6} or from the ^{15}N -labeled azide and triphenylphosphine (eq 1).⁵



Results and Discussion

In Table I are listed the ^{31}P , ^{15}N (obtained from ^{15}N -labeled compounds), and ^{13}C chemical shifts for the series **3a-k**. As was done and discussed previously²⁻⁴ the ^{31}P chemical shifts were measured at three different concentrations (120 mg/3 mL, 80 mg/3 mL, and 40 mg/3 mL) and extrapolated to infinite dilution. Table II shows the various coupling constants including $^1J_{\text{PN}}$ obtained from both the ^{15}N and ^{31}P spectra on the ^{15}N -labeled compounds. There is obviously excellent agreement in $^1J_{\text{PN}}$ obtained both ways. In addition, the numbering scheme used is shown in both tables. Chemical shifts and coupling constants of substituent groups are shown in footnotes in the tables. For compound **3f** the ^{13}C and ^{31}P chemical shifts and PC coupling constants agree reasonably well with the data in the literature.^{7,8}

As we have previously observed in phosphazene- λ^5 -azenes²⁻⁴ the absolute value of the three-bond PC coupling constants are larger than the two-bond coupling constants. Three-bond couplings are often larger than two-bond couplings although this is by no means universal.⁹ In fact the two-bond CF coupling constant in **3g** is larger than the three-bond CF coupling constant, which is similar to what we observed in other phosphazene- λ^5 -azene systems^{2,3} and to what is usually observed.¹⁰ It is interesting to note that the two-bond CN coupling constant through the sp^2 -hybridized carbon, $^2J_{\text{N-C-1}}$, is very much larger than the directly bonded CN coupling constant. A similar observation

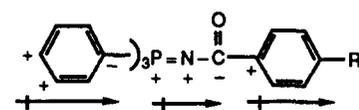


Figure 1. Dipoles induced in **3** when R becomes more electron withdrawing.

was reported for the oxime system $\text{ArCH}=\text{NOH}$ where $|^2J_{\text{NC}}| > |^1J_{\text{NC}}|$.¹¹ This is also a case where a nitrogen is coupled to α and β carbons which are both sp^2 hybridized.

There are a number of linear correlations of the NMR parameters of **3** with various Hammett constants and Taft resonance constants that are suggested by the data. Several of the significant correlations are presented in Table III. All correlations shown are either excellent or satisfactory¹² except $^{13}\text{C-5}$ vs σ_p and the one-bond coupling constants vs σ_p , which are marginal. The ^{31}P , $^{13}\text{C-1'}$, $^{13}\text{C-3'}$, and $^{13}\text{C-4'}$ chemical shifts are all observed to correlate with σ_p . This suggests that, as indicated above, there is no direct overlap between the nitrogen lone pair and the substituent. However, although $\delta_{^{15}\text{N}}$ correlates quite acceptably with σ_p ($r = 0.983$), it also shows an even better, excellent correlation with σ_p^- ($r = 0.995$). It is significant that this correlation, which involves two strongly π -electron-accepting groups, NO_2 and CN , with σ_p^- is so good. It seems to imply that there is significant electron withdrawal from the nitrogen by direct interaction with these electron-withdrawing groups, presumably by way of resonance forms C-F.

Alternatively one can explain this observation as follows. When R is an electron-donating group, the carbonyl withdraws electron density from the ring with less being withdrawn from the phosphazene nitrogen, as in resonance forms C-E. Now, when a strong electron withdrawing group is put onto the ring, more of the nitrogen electrons are donated into the carbonyl such that forms C and F become more important. Thus as R becomes more electron withdrawing the nitrogen becomes more deshielded, an effect that occurs through the π system.

It should also be pointed out that the slopes of the correlation of σ 's with the chemical shifts in the series 1-3 show that the effect of the R group is attenuated in **2** and **3** relative to **1** as would be expected. The similarity of the attenuation in effect of $\delta_{^{31}\text{P}}$, $\delta_{^{13}\text{C-1'}}$, $\delta_{^{13}\text{C-3'}}$, and $\delta_{^{13}\text{C-4'}}$ in the series **2** and **3**, suggests similar mechanisms for this effect. Based on **2**, and the lack of good resonance forms showing direct overlap between the aryl ring and the nitrogen lone pair, the effect appears to be primarily inductive in nature. The effect on the nitrogen chemical shift is different, which, because of the lone pair on nitrogen, is reasonable.^{2,13} There are a number of examples in the literature of substituent effects on ^{15}N chemical shifts being large when there is a free electron pair on nitrogen, and the effect becomes much smaller when this electron pair is removed by protonation¹⁴ or can no longer interact by resonance with the substituent because of steric hindrance.¹⁵

The one-bond coupling constants, $^1J_{\text{PN}}$, $^1J_{\text{PC-1'}}$, and $^1J_{\text{NC-5}}$, show correlations with σ_p where the correlation

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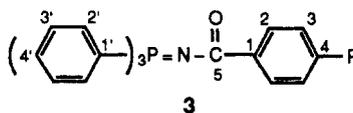
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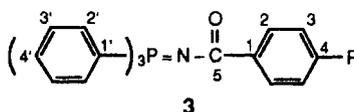
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Table I. ^{13}C , ^{15}N , and ^{31}P NMR Chemical Shifts (ppm) of *N*-Aroyl-*P,P,P*-triphenylphospha- λ^5 -azenes **3**

compd	R	^{13}C									$^{15}\text{N}^a$	$^{31}\text{P}^b$
		1'	2'	3'	4'	5	1	2	3	4		
3a	NMe ₂ ^c	128.87	133.15	128.53	131.96	176.71	126.46	131.07	110.73	152.30		20.02
3b	OBu ^d	128.59	133.14	128.59	132.08	176.07	131.15	131.29	113.34	161.38		20.66
3c	OMe ^e	128.52	133.14	128.60	132.10	175.98	131.38	131.31	112.77	161.75	119.82	20.71
3d	Et ^f	128.48	133.14	128.59	132.10	176.36	136.15	129.61	127.15	147.11		20.81
3e	Me ^g	128.46	133.13	128.60	132.11	176.36	135.87	129.54	128.33	140.76	120.65	20.87
3f	H ^h	128.32	133.13	128.63	132.18	176.26	138.54	129.47	127.62	130.65	121.26	21.19
3g	F	128.22	133.10	128.68	132.25	175.20	134.84	131.73	114.35	164.66	120.93	21.27
3h	Cl	128.10	133.09	128.69	132.29	175.16	137.11	130.95	127.76	136.73	121.68	21.45
3i	Br	128.09	133.10	128.69	132.30	175.25	137.56	131.22	130.74	125.39	121.68	21.48
3j	CN ⁱ	127.64	133.05	128.78	132.49	174.12	142.68	129.94	131.57	113.73	124.12	22.21
3k	NO ₂	127.59	133.08	128.82	132.55	173.87	140.39	130.39	122.89	149.23	124.91	22.27

^a Relative to $^{15}\text{NH}_3(\text{l})$. ^b Extrapolated to infinite dilution and relative to 85% H_3PO_4 . ^c NCH_3 : 40.31. ^d $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$: 67.69, 31.29, 19.29, 13.87, respectively. ^e OCH_3 : 55.28. ^f CH_2CH_3 : 28.87, 15.54, respectively. ^g CH_3 : 21.50. ^h The ^{13}C chemical shifts are in reasonable agreement with those in ref 7 and the ^{31}P chemical shift is in reasonable agreement with that in ref 7 and 8. ⁱ CN: 119.05.

Table II. P-C, C-N, and P-N NMR Coupling Constants (Hz) of *N*-Aroyl-*P,P,P*-triphenylphospha- λ^5 -azenes **3**

compd	R	J_{PC}							J_{CN}			J_{PN}	
		1'	2'	3'	4'	1	2	5	1'	1	5	A ^a	B ^b
3a	NMe ₂	99.3	9.9	12.2	2.9	20.6	2.6	7.8					
3b	OBu	99.5	9.9	12.3	2.8	20.7	2.5	7.8					
3c	OMe	99.5	9.9	12.3	2.9	20.8	2.5	7.8	2.7	13.6	2.6	44.5	44.6
3d	Et	99.4	9.9	12.3	2.9	20.5	2.5	7.9					
3e	Me	99.4	9.9	12.2	2.9	20.5	2.5	8.0	2.6	13.6	2.6	44.7	44.7
3f	H	99.6 ^c	9.9 ^c	12.2 ^c	2.9 ^c	20.6 ^c	2.4 ^c	7.9 ^c	2.6	13.7	2.7	44.6	44.6
3g	F ^d	99.7	9.9	12.3	2.8	21.0	2.5	7.8	2.7	14.0	3.0	44.2	44.2
3h	Cl	99.7	9.9	12.4	2.8	21.0	2.5	7.8	2.5	14.0	2.7	44.1	44.3
3i	Br	99.7	10.0	12.3	2.9	21.0	2.5	7.9	2.5	14.1	2.9	44.0	43.9
3j	CN	99.9	10.0	12.3	2.9	21.2	2.4	7.7	2.7	14.3	3.3	43.8	43.8
3k	NO ₂	100.0	10.0	12.4	2.9	21.3	2.3	7.7	2.6	14.3	3.3	43.8	43.8

^a From ^{31}P spectra. ^b From ^{15}N spectra. ^c These J_{PC} values are in reasonable agreement with those in ref 7. ^d $^1J_{\text{FC-4}} = 249.3$, $^2J_{\text{FC-3}} = 21.5$, $^3J_{\text{FC-2}} = 8.8$, $^4J_{\text{FC-1}} = 2.8$.

Table III. Linear Relationships between NMR Parameters of *N*-Aroyl-*P,P,P*-triphenylphospha- λ^5 -azenes **3** and Substituent Constants

plot of x vs y				
y	x	slope	correltn coeff	no. of points
$^{13}\text{C-1}$ SCS	$\sigma_{\text{R}}^{\circ}$	22.7	0.973	11
$^{13}\text{C-5}$ SCS	σ_{p}^{-a}	-1.59	0.945	11
$^{13}\text{C-1'}$ SCS	σ_{p}	-0.900	0.997	11
$^{13}\text{C-3'}$ SCS	σ_{p}	0.198	0.983	11
$^{13}\text{C-4'}$ SCS	σ_{p}	0.411	0.991	11
^{15}N SCS	σ_{p}^{-}	3.23	0.995	8
^{31}P SCS	σ_{p}	1.53	0.994	11
$^1J_{\text{PC-1'}}$	σ_{p}	0.473	0.948	11
$^1J_{\text{PN}}$	σ_{p}	-0.828	0.902	8
$^1J_{\text{NC-5}}$	σ_{p}	0.686	0.909	8

^a σ_{p}^{-} values were used for *p*-NO₂ and *p*-CN. Since σ_{p} is the same as σ_{p}^{-} for the other substituents, σ_{p} values were used for these.

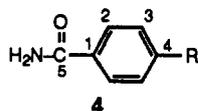
coefficients, r , are somewhat below what is considered acceptable ($r = 0.95$), but there are clear trends. Unfortunately the overall range of 1J from the one end of the scale to the other is only 0.7–0.8 Hz and an involved explanation can not be justified.

It should be noted, however, that as was the case with series 1, as $^1J_{\text{PN}}$ increases, $^1J_{\text{PC}}$ decreases, and $^1J_{\text{PN}}$ decreases with the electron-withdrawing ability of the sub-

stituent. This is consistent with our earlier suggestion³ that such electron-withdrawing groups decrease the extent of both $p\pi$ - $d\pi$ and $p\pi$ - σ^* bonding. Consequently, $^1J_{\text{PN}}$ decreases due to decreased PN bonding and $^1J_{\text{PC}}$ increases due to less $p\pi$ - σ^* bonding.

Based on the observation that $^1J_{\text{NH}}$ in a series of substituted anilines increased with more strongly electron withdrawing groups, it was suggested that this increase is simply a manifestation of greater s character in the N-H bond due to more double-bond character between the nitrogen and ring carbon.¹⁶ This is opposite to what we observe with the one-bond PN coupling constants in series 1–3²⁻⁴ and so an analogous effect can be ruled out.

There is another electrostatic argument, which can also explain the trends in $^1J_{\text{PN}}$ and $^1J_{\text{PC-1'}}$. In Figure 1 are shown the dipoles induced in **3** when the substituent R is made more electron withdrawing. The signs on each atom is the sign of the SCS Hammett ρ value for each nucleus, and so a positive sign represents deshielding by the more electron-withdrawing R group. Thus, based on electrostatics only, we can predict that both the P-C-1' and N-C-5 bonds should shorten due to attraction while the

Table IV. ^{13}C and ^{15}N NMR Chemical Shifts (ppm) of Para-Substituted Benzamides 4 in Me_2SO 

R	$^{13}\text{C}^a$					$^{15}\text{N}^{b,c}$
	1	2	3	4	5	
OMe ^d	127.27	130.24	114.20	162.46	168.58	100.50
Me ^e	132.24	128.37	129.55	141.94	168.94	101.36
H	135.02	128.33	129.03	132.08	169.05	102.16
F ^f	131.43	130.93	115.81	164.77	167.98	102.11
Cl	133.80	130.24	129.08	137.03	167.87	102.69
Br	134.24	130.50	132.10	125.96	167.95	102.68
CN ^g	139.09	129.14	133.16	114.58	167.49	104.61
NO ₂	140.79	129.78	124.25	149.88	167.20	105.13

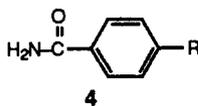
^aThe ^{13}C -1- ^{13}C -4 chemical shifts are in reasonable agreement with those in ref 18 and 19 and the ^{13}C -5 chemical shifts are in reasonable agreement with those in Bromilow, J.; Brownlee, R. T. C.; Craik, D. J.; Fiske, P. R.; Rowe, J. E.; Sadek, M. J. *Chem. Soc., Perkin Trans. 2* 1981, 753. ^bRelative to ^{15}N chemical shifts are in reasonable agreement with those in ref 17. ^c OCH_3 : 56.03. ^d CH_3 : 21.72. ^e $^1J_{\text{FC-4}} = 248.8$ Hz. ^f $^1J_{\text{FC-2}} = 9.0$ Hz, $^4J_{\text{FC-1}} = 2.9$ Hz. ^gCN: 119.20

Table V. Linear Relationships of ^{13}C and ^{15}N Chemical Shifts between *N*-Aroyl-*P,P,P*-triphenylphospha- λ^5 -azenes 3 and Para-Substituted Benzamides 4

chem shift of atom	plot of x vs y		slope	correlation coeff (r)	no. of points
	x	y			
^{13}C -1	4	3	0.976	0.998	8
^{13}C -2	4	3	0.861	0.981	8
^{13}C -3	4	3	1.002	1.000	8
^{13}C -4	4	3	1.001	1.000	8
^{13}C -5	4	3	1.352	0.974	8
^{15}N	4	3	1.114	0.989	8

$\text{P}=\text{N}$ bond should lengthen due to repulsion. A shortened bond will increase the s character of the atomic orbitals used to form the bond and hence the one-bond coupling constants will increase ($^1J_{\text{PC-1}}$ and $^1J_{\text{NC-5}}$). In contrast, a lengthened bond will decrease the s character of the atomic orbitals and hence will decrease the coupling constant ($^1J_{\text{PN}}$). This is exactly what is observed, i.e., the Hammett values for plots of 1J vs σ_p are positive for $^1J_{\text{PC-1}}$ and $^1J_{\text{NC-5}}$ and negative for $^1J_{\text{PN}}$.

Since it appears that there is little direct resonance interaction of the substituent with the nitrogen atom, and the effect of the PN and PC bonding as determined by the one-bond coupling constants is relatively small, we decided to examine the corresponding benzamide series (4). All compounds in series 4 were synthesized with an ^{15}N label.



- a: R = OMe d: R = F g: R = CN
 b: R = Me e: R = Cl h: R = NO₂
 c: R = H f: R = Br

Table IV shows the ^{15}N and ^{13}C chemical shifts for this series, 4, and all are in reasonable agreement with those reported.¹⁷⁻¹⁹ Table V shows the correlations of the chemical shifts of the carbon and nitrogen atoms in series 3 with those in series 4. The positively charged phosphorus

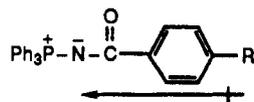


Figure 2. Dipole induced in 3 by the addition of a triphenylphosphonium group to 4.

Table VI. Taft DSP Analyses of SCS in *N*-Aroyl-*P,P,P*-triphenylphospha- λ^5 -azenes 3

nucleus	ρ_I	ρ_R	scale ^a	f^b	no. of points
^{13}C -1	4.8	20.8	$\sigma_{\text{R}}^{\circ}$	0.07	11
^{13}C -5	-3.0	-1.2	σ_{R}^{-}	0.10	11
^{13}C -1'	-0.92	-1.1	$\sigma_{\text{R}}^{\circ}$	0.09	11
^{13}C -1''	-0.94	-0.79	$\sigma_{\text{R}}^{\text{BA}}$	0.08	11
^{13}C -3'	0.23	0.22	$\sigma_{\text{R}}^{\circ}$	0.07	11
^{13}C -4'	0.45	0.49	$\sigma_{\text{R}}^{\circ}$	0.05	11
^{15}N	2.7	4.2	σ_{R}^{-}	0.08	8
^{31}P	1.4	2.1	$\sigma_{\text{R}}^{\circ}$	0.09	11
$^1J_{\text{PN}}$	-1.3	-0.39	$\sigma_{\text{R}}^{\text{BA}}$	0.11	8
$^1J_{\text{PC-1'}}$	0.49	0.60	$\sigma_{\text{R}}^{\circ}$	0.23	11

^aThe correlations were done for each of the four resonance scales ($\sigma_{\text{R}}^{\circ}$, $\sigma_{\text{R}}^{\text{BA}}$, σ_{R}^{+} , and σ_{R}^{-}), and the results for the one with the lowest f (best fit) are shown. ^b $f = \text{SD}/\text{rms}$.

of the phosphazanyl group clearly polarizes the rest of the molecule (N, CO, and aryl groups) relative to the benzamides. This can be seen first by the observation that the phosphorus deshields the nitrogen in 3 by 18.9–19.8 ppm, the carbonyl carbon (C-5) by 6.6–7.4 ppm, and carbon atoms 1 and 2 by 3.3–4.1 (except for 3k) and 0.6–1.2 ppm, respectively, compared to the corresponding atoms in 4. On the other hand, carbon atoms 3 and 4 in 3 are shielded by 1.2–1.6 and 0.1–1.4 ppm, respectively. Thus, overall, the $\text{NC}(\text{O})\text{C}_6\text{H}_4\text{R}$ group can be considered a unit and the extra effect of the positively charged phosphorus can be shown diagrammatically by the dipole in Figure 2.

Furthermore, plots of the ^{13}C and ^{15}N chemical shifts in 3 vs those in 4 all gave good to excellent correlations (Table V). The slopes for C-3 and C-4 were essentially unity; however, the slopes for C-1 and C-2 were less than unity (C-1 and C-2 in 3 are less responsive to R) while for C-5 and N they were greater than unity (C-5 and N in 3 are more responsive to R). This is consistent with what was shown in Figure 1 and the discussion above. That is, N and C-5 act together and the aromatic ring acts as a unit. This latter response is due to the greater negative charge on N and C-5 in 3, which, as we pointed out, also gives rise to greater shielding of these atoms in 3.

As has frequently been done with disubstituted benzenes, we examined the Taft DSP treatment (eq 3) for the

$$\text{substit. effect} = \sigma_I \rho_I + \sigma_R \rho_R \quad (3)$$

substituent chemical shift and coupling constant effects.²⁰ The substituent effect shown in eq 3 is defined as δ (or J) for the substituent minus δ (or J) for a hydrogen substituent. Table VI shows the best fits using $\sigma_{\text{R}}^{\circ}$, $\sigma_{\text{R}}^{\text{BA}}$, and σ_{R}^{-} along with σ_I . In the case of the chemical shift correlations all are excellent ($f < 0.1$; $f = \text{SD}/\text{rms}$), except for C-5, $^1J_{\text{PN}}$ and $^1J_{\text{PC-1}}$, where the correlations are good ($f < 0.2$). Once again, however, since the range of coupling constants is small, the poorer fits are not surprising. Except for C-1, the chemical shift effects show that the inductive and resonance effects contribute equally to within a factor of about 2 (slightly greater than 2 with C-5). For C-1 the resonance effect is 4–5 times more important than the inductive effect in agreement with many 1,4-disubstituted benzenes.²⁰ In fact the value for ρ_R and ρ_I of 20.8

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Table VII. DSP and DSP-NLR Analyses of ¹³C-1 SCS in 1-6

series	ε	ρ _I	ρ _R	f	s.d.	no. of points
1 ^a	none	7.0	19.6	0.16	7.39	9
1 ^a	1.10	5.7	27.3	0.08	1.56	9
5 ^b	none	5.0	17.8	0.14	0.67	14
5 ^b	0.56	4.1	21.0	0.06	0.28	14
2 ^c	none	4.4	20.4	0.06	0.82	10
2 ^c	-0.25	4.8	18.6	0.02	0.15	10
6 ^c	none	4.2	19.3	0.13	2.20	10
6 ^c	-0.65	4.8	15.8	0.04	0.20	10
3	none	4.8	20.8	0.07	1.63	11
3	-0.35	4.7	17.9	0.03	0.35	11
4	none	4.7	20.0	0.08	0.73	8
4	-0.40	5.0	17.9	0.03	0.10	8

^aTaken from ref 3. ^bTaken from ref 20. ^cTaken from ref 2.

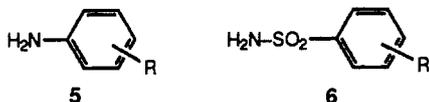
and 4.8 in 3 are very nearly identical with the corresponding values of 21.9 and 4.9 for the benzamide series 4 reported by Brownlee and Sadek¹⁹ and our values of 20.0 and 4.7 ($f = 0.08$) for 4, respectively. This also points up the electronic similarities between the NH₂ group and the triphenylphosphazene group.

It is also interesting to note that for both the N and C-5 chemical shifts the best correlations are with σ_R^- , again suggesting that there is some delocalization from the NCO group into the aromatic ring.

When two groups are para to each other and can mutually interact, it has been suggested^{19,20} that a nonlinear resonance relationship be used (eq 4) for the ipso carbon (C-1 in our systems), where there is now an effective res-

$$\text{C-1 SCS} = \sigma_{IP1} + [\sigma_R^0 \rho_R / (1 - \epsilon \sigma_R^0)] \quad (4)$$

onance parameter $\bar{\sigma}_R = \sigma_R^0 / (1 - \epsilon \sigma_R^0)$. The mutual interactions will depend on the electron demand placed on one group by the other. Since the effective σ_R should become larger when one group is electron donating while the other is electron withdrawing, the value for ϵ should be greatest when strongly electron withdrawing or donating groups are used as the fixed group. Table VII shows the best values for ϵ using the C-1 substituent chemical shift (SCS) in the series 1,³ 2,² 3, 4, the anilines 5,¹⁹ and sulfonamides 6,² along with the normal DSP treatment pa-



rameters and the Taft f parameter and standard deviation. It should be noted that our value of ϵ for series 4 agrees with the value of -0.48 reported.¹⁹

If the magnitude of ϵ is thought of as a rough index of the strength of the electron-donating or -withdrawing ability of the fixed group, it is clear that the Ph₃P=N group is strongly electron donating and is even more electron donating than NH₂. The Ph₃P=NSO₂ group is moderately electron withdrawing while H₂N-SO₂ is much more strongly electron withdrawing. This, of course, is consistent with the formal negative charge on the nitrogen in 2 attenuating the strong electron withdrawing ability of SO₂NH₂ in 6. However, the Ph₃P=NC(O) and H₂NC(O) groups both appear to be about equally moderately electron withdrawing with the former in 3 being a little less electron withdrawing than the latter in 4. The smaller difference in these groups compared to Ph₃P=NSO₂ and NH₂SO₂ may be related to the ability of the nitrogen to interact more strongly with the ring in 3 *vide supra* causing some back donation to the aromatic ring and reducing the electron-withdrawing ability of Ph₃P=NC(O) relative to NH₂C(O).

Experimental Section

General. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. IR spectra were recorded on either a Perkin-Elmer 599B dispersive or a Biorad-Digilab Fourier transform spectrometer using KBr pellets. NMR spectra were recorded in CDCl₃ solvent and 12-mm tubes on a Nicolet NT-200 WB spectrometer with a 4.7 T superconducting solenoid, at 200.07 MHz for ¹H, 80.99 MHz for ³¹P, 50.31 MHz for ¹³C, and 20.28 MHz for ¹⁵N. Some proton spectra were obtained at 60 MHz on a Varian T-60 NMR spectrometer. The ³¹P spectra were recorded with use of an external (concentric 5-mm tube) 85% H₃PO₄ standard, with concentrations of 120 mg/3 mL, 80 mg/3 mL, and 40 mg/3 mL for 3, and the reported chemical shifts were extrapolated to infinite dilution. Two-level broad band proton decoupling was employed with a pulse angle of approximately 90° and a post acquisition delay of 1 s. The data were collected using 16K data points, zero filled to 32K, and processed without exponential line broadening. The sweep width was 3610 Hz. The ¹³C spectra were obtained using (CH₃)₄Si as internal standard and a concentration of 120 mg/3 mL for 3 and 150 mg/0.5 mL of Me₂SO in 5-mm tubes for the benzamides (4). These tubes were put in a 12-mm concentric tube containing CDCl₃ for lock. Two-level broad band proton decoupling was employed, a pulse angle of about 23° and a post acquisition delay of 10 s. The data were collected by using 32K data points and a total sweep width of 11 100 Hz and was processed by zero filling to 64K data points. No exponential line broadening was employed. The ¹⁵N spectra were obtained by using gated, broad-band proton decoupling (decoupler on during acquisition), a pulse angle of about 23°, and a post acquisition delay of 6 s. For the phosphazenes 3, an external standard (concentric 5-mm tube) of a solution of K¹⁵NO₃ in H₂O, which had been standardized against neat CH₃NO₂, was used and chemical shifts relative to NH₃(l) were calculated by using $\delta(\text{NH}_3) = \delta(\text{CH}_3\text{NO}_2) + 380.23$.²¹ The data were collected by using 32K data points and a total sweep width of 14 KHz and were processed by zero filling to 64K data points. No exponential line broadening was employed. For 3 the concentrations were between 150 and 200 mg/3 mL of CDCl₃ while for the benzamides (4) it was 100 mg/0.6 mL of Me₂SO except for the *p*-NO₂ derivative 4h, which was 30 mg/0.4 mL of Me₂SO. These tubes were put into a concentric 12-mm tube containing CDCl₃. The internal 5-mm tube was then replaced by the standard K¹⁵NO₃/H₂O sample (5-mm tube) and the chemical shift difference was obtained and then related to NH₃(l) as described above. Elemental analyses were determined by Galbraith Laboratories, Knoxville, TN, or Texas Analytical Laboratories, Houston, TX, and Tallahassee, FL.

N-Aroyl-*P,P,P*-triphenylphosphazene 3. General. Two different procedures were employed for the syntheses of the derivatives of 3.

Procedure A.⁶ To a stirred and cooled solution of the benzamide (1 or 2 mmol) and triphenylphosphine (1 or 2 mmol) in dry tetrahydrofuran (5 or 10 mL; distilled from LiAlH₄) under dry argon was added diethyl azodicarboxylate (1 or 2 mmol) dropwise, by syringe, through a rubber septum. The solution was allowed to warm to room temperature and was stirred for 12 h. The solvent was removed under vacuum, 2 mL of MeOH was added, and the solid that formed was filtered and recrystallized from the solvent indicated.

Procedure B.²² To a cold (5–10 °C), stirred solution of triphenylphosphine in dry tetrahydrofuran (distilled from LiAlH₄) was added, dropwise, the aroyl azide, prepared from the corresponding aroyl chloride and sodium azide,^{23,24} in dry tetrahydrofuran. The mixture was stirred for 4 additional hours, warmed to 40 °C, and stirred for 1 more h. The solvent was removed under vacuum and the residue was recrystallized from the indicated solvent.

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Compounds **3c,e-k** were prepared as described previously⁵ by procedures B, B, A, B, B, A, and A, respectively.

N-[p-(Dimethylamino)benzoyl]-P,P,P-triphenylphospha-λ⁵-azene (3a). Procedure B was used. From 0.27 g of *p*-(dimethylamino)benzoyl azide (1.4 mmol) and 0.38 g (1.4 mmol) of triphenylphosphine in 10 mL of dry THF was obtained, after recrystallization from chloroform-hexane, 0.20 g (34%) of product; mp 135-137 °C. IR (KBr): $\bar{\nu}$ (cm⁻¹) 3051, 2889 (C-H), 1601, 1582 (C=O), 1331 (P=N). ¹H NMR (CDCl₃): δ 3.01 (s, 6 H, NCH₃), 6.69 (d, 2 H, Ar H, *J* = 8.8 Hz), 7.4-7.7 (m, 9 H, Ar H), 7.8-8.0 (m, 6 H, Ar H), 8.25 (d, 2 H, Ar H, *J* = 8.8 Hz). Anal. Calcd for C₂₇H₂₅N₂OP: C, 76.40; H, 5.94; N, 6.60. Found: C, 76.37; H, 5.96; N, 6.47.

N-(p-Butoxybenzoyl)-P,P,P-triphenylphospha-λ⁵-azene (3b). Procedure B was used. From 1.10 g (5.1 mmol) of *p*-butoxybenzoyl azide and 1.31 g (5.0 mmol) of triphenylphosphine in 15 mL of dry THF was obtained 2.15 g (95%) of **3b**, mp 152-155 °C. After recrystallization from benzene-petroleum ether, 1.90 g (84%) of **3b** was obtained, mp 154-156 °C. IR (KBr): $\bar{\nu}$ (cm⁻¹) 3060, 2960, 2920 (C-H), 1592 (C=O), 1328 (P=N). ¹H NMR (CDCl₃): δ 0.96 (t, 3 H, CH₃, *J* = 6 Hz), 1.43 (m, 2 H, CH₂), 1.73 (m, 2 H, CH₂), 3.98 (t, 2 H, OCH₂, *J* = 5 Hz), 6.91 (d, 2 H, Ar H, *J* = 8 Hz), 7.46 (m, 9 H, Ar H), 7.85 (m, 6 H, Ar H), 8.32 (d, 2 H, Ar H, *J* = 8 Hz). Anal. Calcd for C₂₉H₂₈NO₂P: C, 76.80; H, 6.22; N, 3.09. Found: C, 77.06; H, 6.42; N, 3.00.

N-(p-Ethylbenzoyl)-P,P,P-triphenylphospha-λ⁵-azene (3d). Procedure B was used. From 1.75 g (10.2 mmol) of *p*-ethylbenzoyl azide and 2.62 g (10.0 mmol) of triphenylphosphine

in 25 mL of dry THF was obtained 3.88 g (95%) of **3d**, mp 133-136 °C. After recrystallization from methanol, 3.34 g (82%) of **3d** was obtained, mp 135-137 °C. IR (KBr): $\bar{\nu}$ (cm⁻¹) 3060, 2962 (C-H), 1592 (C=O), 1550 (Ar), 1325 (P=N). ¹H NMR (CDCl₃): δ 1.21 (t, 3 H, CH₃, *J* = 7.6 Hz), 2.64 (q, 2 H, CH₂, *J* = 7.6 Hz), 7.19 (d, 2 H, Ar H, *J* = 8.0 Hz), 7.42 (m, 9 H, Ar H), 7.80 (m, 6 H, Ar H), 8.29 (d, 2 H, Ar H, *J* = 8.1 Hz). Anal. Calcd for C₂₇H₂₄NO: C, 79.20; H, 5.91; N, 3.42. Found: C, 79.44; H, 6.06; N, 3.32.

¹⁵N-labeled **3** was prepared as above by using either ¹⁵N-labeled benzamides²⁵ (procedure A) or ¹⁵N-labeled aryl azides (procedure B).²⁶ The yields and melting points of the labeled compounds are as follows: **3c**, R = OCH₃, 63%, 158-160 °C; **3e**, R = CH₃, 73%, 153-155 °C; **3f**, R = H, 36%, 190-195 °C; **3g**, R = F, 52%, 178-180 °C; **3h**, R = Cl, 53%, 146-150 °C; **3i**, R = Br, 61%, 145-146 °C; **3j**, R = CN, 62%, 178-179 °C; **3k**, R = NO₂, 74%, 201-205 °C.

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(26) The labeled aryl azides were made by standard methods from the aryl chloride and ¹⁵N-labeled sodium azide in THF/H₂O (2:1).²⁴

Rapid Continuous Peptide Synthesis via Fmoc Amino Acid Chloride Coupling and 4-(Aminomethyl)piperidine Deblocking

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The recently described Fmoc/4-AMP technique for rapid continuous solution synthesis of peptides involving coupling by crystalline Fmoc amino acid chlorides and deblocking via 4-(aminomethyl)piperidine (4-AMP) has been extended to the synthesis of a varied number of tachykinin peptides. Previously only the simple pentapeptide leucine enkephalin had been synthesized by this procedure. Continuous syntheses of peptides up to the heptapeptide stage have been executed in a single repetitive operation. Removal of excess acid chloride during the coupling step was simplified by use of 4-AMP for this purpose as well as for the deblocking step. Use of this modified technique gave purer crude products and higher yields. A method of avoiding complications due to the interfering separation of solid material during the washings with phosphate buffer to remove byproducts was developed based on the use of chloroform. Crude products obtained by the modified procedure were often of greater than 95% purity. Segments bearing proline at the C-terminal position required special attention due to diketopiperazine formation at the dipeptide stage. Such diketopiperazines were avoided with both proline amides and proline *tert*-butyl esters. Using the latter technique Z-Arg(NO₂)-Pro-Lys(Z)-Pro-OH, **9**, was synthesized and coupled with H- δ -Ava-Phe-Phe-Gly-Leu-Nle-NH₂, **6**, obtained via benzyl esters, to give the undecapeptide Substance P analogue **10**, which was also synthesized by solid-phase methods for comparison. MS/FAB and NMR data are presented for selected peptides synthesized by these new rapid procedures.

Recently we described in preliminary form a new technique for the rapid, multigram synthesis of short peptide segments.^{1,2} Both coupling and deblocking steps were novel, the former being based on a new class of stable,

highly reactive coupling agents, Fmoc amino acid chlorides, and the latter involving reaction with 4-(aminomethyl)piperidine (4-AMP), a difunctional amine chosen to facilitate efficient removal of byproducts. The previous paper emphasized the preparation and characterization of the Fmoc amino acid chlorides; here we provide experimental details along with a description of modifications of the basic technique leading to greater reliability and convenience. According to the original protocol (Table I, protocol A) excess acid chloride is scavenged following the initial rapid acylation reaction in a chloroform-water

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