Poly(tertiary phosphines and arsines). XIII. Some Neopentyl Poly(tertiary phosphines)[1,2]

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Reaction of $(Me_3CCH_2)_2PH$ with $(Me_3CCH_2)_2PCH{=}CH_2$ in boiling toluene in the presence of potassium *tert*-butoxide gives the crystalline neopentyl di(tertiary phosphine) $(Me_3CCH_2)_2PCH_2CH_2P(CH_2CMe_3)_2$. A similar base-catalyzed reaction of $C_6H_5PH_2$ with $(Me_3CCH_2)_2PCH{=}CH_2$ in boiling tetrahydrofuran gives the liquid tertiary–secondary diphosphine $C_6H_5P(H)CH_2CH_2P(CH_2CMe_3)_2$. Base-catalyzed reaction of 2 equiv of $(Me_3CCH_2)_2PH$ with $Me_3CCH_2P(S)(CH{=}CH_2)_2$ in boiling tetrahydrofuran followed by desulfurization with sodium in boiling dioxane gives the viscous liquid neopentyl tri(tertiary phosphine) $Me_3CCH_2P[CH_2CH_2P(CH_2CMe_3)_2]_2$. Base-catalyzed reaction of phosphine with $(Me_3CCH_2)_2P(S)CH{=}CH_2$ gives the tetraphosphine trisulfide $P[CH_2CH_2P(S)(CH_2CMe_3)_2]_3$ which undergoes desulfurization with sodium metal in boiling dioxane to give the neopentyl tripod tetra(tertiary phosphine) $P[CH_2CH_2P(CH_2CMe_3)_2]_3$. The proton, phosphorus-31, and carbon-13 NMR spectra of these new neopentyl polyphosphines as well as the related neopentylphosphorus derivatives $(Me_3CCH_2)_3P$, $(Me_3CCH_2)_2P(O)H$, $(Me_3CCH_2)_nPX_{3-n}$ (n = 1 and 2; X = H, Cl, C_6H_5, and $CH{=}CH_2$), $(Me_3CCH_2)_3PS$, and $(Me_3CCH_2)_nP(S)R_{3-n}$ (n = 1 and 2; R = C_6H_5 and $CH{=}CH_2$) are described.

Previous papers of this series describe the preparation of poly(tertiary phosphines) in which the phosphorus atoms are linked by $-CH_2CH_2-$ bridges with the terminal positions on each phosphorus atom occupied by phenyl[5] and methyl[6] groups. Subsequent papers[1,7,8,9] describe extensive series of transition metal complexes formed by these phosphines.

In order to complement the donor properties of the methyl and phenyl poly(tertiary phosphines) toward transition metals, we were interested in obtaining analogous poly(tertiary phosphines) with terminal neopentyl groups. A neopentyl group [i.e., $(CH_3)_3CCH_2-$] provides a reasonable electronic approximation to a methyl group but is more sterically demanding than not only a methyl group but also even a phenyl group. For such reasons a comparison of the coordination chemistry of neopentyl poly(tertiary phosphines) with that of phenyl and methyl poly(tertiary phosphines) might provide a basis for differentiating between steric and electronic effects in this area of coordination chemistry. Furthermore, the neopentyl group, unlike the phenyl group but like the methyl group, has reasonably simple proton and carbon-13 NMR spectra thereby providing potentially useful probes for characterizing metal complexes.

Neopentylphosphorus chemistry relevant to the construction of poly(tertiary phosphines) with terminal neopentyl groups is rather obscure, although diphenylneopentylphosphine[10] has been described in the literature. For this reason, our synthetic objective of neopentyl poly(tertiary phosphines) first required the development of reliable and efficient procedures for preparing the necessary building blocks containing one phosphorus atom before methods of combining these building blocks to form the polyphosphines could be investigated. After obtaining the necessary neopentylphosphorus derivatives with only one phosphorus atom, exploration of various methods of combining such units led to the syntheses of the neopentyl di(tertiary phosphine) $(Me_3CCH_2)_2PCH_2CH_2P(CH_2CMe_3)_2$, the tri(tertiary phosphine) $Me_3CCH_2P[CH_2CH_2P(CH_2CMe_3)_2]_2$, and the tripod tetra(tertiary phosphine) $P[CH_2CH_2P(CH_2CCMe_3)_2]_3$. Since the synthetic methods employed in this work involve some problems not previously encountered in the earlier work with methyl[6] and phenyl[5] poly(tertiary phosphines), they are discussed in detail in this paper along with the NMR spectra of the new neopentylphosphorus derivatives.

Results and Discussion

A. Syntheses. In these syntheses of neopentyl poly(tertiary phosphines) the following features are of particular interest: (1) The lower reactivity of the neopentylphosphorus systems toward the base-catalyzed addition reactions. In some cases, conversion of a neopentylvinylphosphine into the corresponding sulfide is necessary in order to make the vinylphosphorus system acceptably reactive toward the phosphorus–hydrogen compound. The purpose of the sulfurization of neopentylvinylphosphines to increase their reactivity toward such addition reactions contrasts with the purpose of the previously used[6] sulfurization of methylvinylphosphines in order to make the methylphosphorus systems more readily prepared and handled. (2) Difficulties in desulfurizing some neopentylphosphine sulfides with $LiAlH_4$ making it necessary to use the more reactive sodium metal. Sodium metal is an unacceptable reagent for desulfurizing many organophosphorus sulfides, however, because of the possibility of unwanted carbon–phosphorus bond cleavage to give alkali metal phosphides,[11] particularly in the case of arylphosphorus derivatives. Neopentyl–phosphorus bonds as well as PCH_2CH_2P units in neopentylphosphorus derivatives seem to be reasonably resistant to cleavage with sodium metal in dioxane, although the reaction conditions (concentration, time, temperature, etc.) for the sodium metal desulfurizations described in this paper seem to be relatively critical possibly owing to detrimental carbon–phosphorus bond cleavage if the reaction conditions are too vigorous.

These special features of neopentylphosphorus chemistry probably arise from the steric bulk of the neopentyl group. This bulk of the neopentyl group may be responsible for other special properties of neopentylphosphines such as their lower sensitivity toward oxidation relative to other alkylphosphines [tris(neopentylphosphine) seems to be about as air stable as triphenylphosphine] and the unusual odors of many trivalent neopentylphosphorus compounds which are very different from the atrocious odors of most volatile trivalent phosphorus derivatives. Nevertheless, the neopentylphosphorus derivatives $Me_3CCH_2PCl_2$, $(Me_3CCH_2)_2PCl$, $Me_3CCH_2PH_2$, and $(Me_3CCH_2)_2PH$ were so sensitive to air oxidation and hydrolysis that their elemental analyses caused difficulties. However, the NMR spectra as well as the chemical reactions of these four compounds provided positive proof of their identities.

Table I. Neopentylphosphorus Derivatives Prepared in This Work

Registry no.	Compd[a]	Preparation[b]	Yield, %	Mp or bp (mm),[c] °C		Anal, %			^{31}P NMR[d]	
						C	H	Other	Found	Calcd[e]
57620-64-1	Neo$_3$P	3NeoMgCl + PCl$_3$ in THF	27	57–59	Calcd	73.7	13.6	12.7 (P)	+57.5 s	+54
				75–80 (0.2)	Found	73.8	13.5	12.4 (P)		
57620-65-2	Neo$_2$P(O)H	Hydrolysis of 3NeoMgCl + PCl$_3$	23	69–71	Calcd	63.1	12.1		−21.5 (J_{PH} = 455 Hz)[i]	
					Found	63.1	12.2			
57620-66-3	Neo$_2$PCl	2NeoMgCl + PCl$_3$ in Et$_2$O	74	49–50 (0.4)	Calcd[f]	57.5	10.5	17.0 (Cl)	−102.3 s	
				110 (25)	Found[f]	55.4	10.3	16.3 (Cl)		
57620-67-4	NeoPCl$_2$	NeoMgCl + PCl$_3$ in Et$_2$O	67	57–65 (25)	Calcd[f]	34.7	6.4	41.0 (Cl)		
					Found[f]	36.3	6.5	37.1 (Cl)		
57620-68-5	Neo$_2$PPh	2NeoMgCl + PhPCl$_2$	64	93–95 (0.2)	Calcd	76.8	10.8	12.4 (P)	+42.2	+39
					Found	76.6	10.6	12.2 (P)		
7660-85-7	NeoPPh$_2$	NeoMgCl + Ph$_2$PCl in THF	68	125–130 (0.2)		g			+23.6 s	+24
				116–122 (0.1)[h]					(+23.9)[h]	
57620-69-6	Neo$_2$PVi	ViMgBr + Neo$_2$PCl in THF	80	38 (0.3)	Calcd	72.0	12.5	15.5 (P)	+44.8 s	+42
				110 (32)	Found	72.2	12.7	15.6 (P)		
57620-70-9	NeoPVi$_2$	2ViMgBr + NeoPCl$_2$ in THF	55	72 (28)	Calcd	69.2	11.0	19.8 (P)	+31.9 s	+30
					Found	69.2	11.0	20.0 (P)		
57620-71-0	Neo$_3$P(S)	Neo$_3$P + S	91	169–171	Calcd	65.2	11.9	11.6 (S)	−36.9 s	
					Found	65.0	12.1	11.5 (S)		
57620-72-1	Neo$_2$P(S)Ph	Neo$_2$PPh + S	76	105–107	Calcd	68.0	9.6	11.3 (S)	−34.9 s	
					Found	67.8	9.6	11.4 (S)		
57620-73-2	NeoP(S)Ph$_2$	NeoPPh$_2$ + S	86	134–135	Calcd	70.9	7.3	11.1 (S)	−35.6 s	
					Found	70.7	7.4	10.9 (S)		
57620-74-3	Neo$_2$P(S)Vi	Neo$_2$PVi + S	98	89–90	Calcd	62.1	10.8	13.8 (S)	−33.1 s	
					Found	62.2	10.9	14.0 (S)		
57620-75-4	NeoP(S)Vi$_2$	NeoPVi$_2$ + S	95	19	Calcd	57.4	9.1	17.1 (S)	−30.9 s	
					Found	57.5	9.1	17.0 (S)		
57620-76-5	Neo$_2$PH	Neo$_2$PCl + LiAlH$_4$	64	57 (5)	Calcd	69.0	13.2	17.8 (P)	+98.1 (J_{PH} = 189 Hz)[i]	
					Found	69.1	13.5	17.4 (P)		
54772-70-2	NeoPH$_2$	NeoPCl$_2$ + LiAlH$_4$	52	98–100 (760)	Calcd[f]	57.5	12.5	29.8 (P)	+162.4	
					Found[f]	59.4	12.8	26.3 (P)		
57620-77-6	Neo$_2$PCH$_2$CH$_2$PNeo$_2$	Neo$_2$PH + Neo$_2$PVi	63	66–68	Calcd	70.6	12.8	16.6 (P)	+42.6 s	+43
					Found	70.7	13.1	16.4 (P)		
57620-78-7	Neo$_2$PCH$_2$CH$_2$P(S)-Me$_2$	Neo$_2$PH + Me$_2$P(S)Vi	11	133–134	Calcd	57.1	11.0	10.9 (S)	+42.7 d (35)	+43
					Found	57.1	10.9	11.0 (S)	−38.1 d (35)	
57620-79-8	PhP(H)CH$_2$CH$_2$-PNeo$_2$	PhPH$_2$ + Neo$_2$PVi	27	125–140 (0.2–0.8)	Calcd	69.7	10.3	20.0 (P)	+46.0 (J_{PH} = 192 Hz)[i]	+43
					Found	69.7	10.6	19.7 (P)	+43.7	
57620-80-1	PhP[CH$_2$CH$_2$P(S)-Neo$_2$]$_2$	PhPH$_2$ + 2Neo$_2$P(S)Vi	86	138	Calcd	62.8	10.0	11.1 (S)	+17.1 t (37)	+17
					Found	62.7	10.1	11.2 (S)	−42.7 d (37)	
57620-81-2	NeoP[CH$_2$CH$_2$PNeo$_2$]$_2$	See text	58	Liquid	Calcd	69.0	12.6	18.4 (P)	+43.0 d (20)	+43
					Found	67.7	12.3	17.7 (P)	+30.6 t (20)	+33
57620-82-3	P[CH$_2$CH$_2$P(S)Neo$_2$]$_3$	PH$_3$ + 3Neo$_2$P(S)Vi	95	237	Calcd	59.1	10.7	13.2 (S)	+18.1 q (32)	+21
					Found	59.0	10.7	13.2 (S)	−43.6	
57620-83-4	P(CH$_2$CH$_2$PNeo$_2$)$_3$	P[CH$_2$CH$_2$P(S)Neo$_2$]$_3$ + Na in dioxane	65	77–81	Calcd	68.1	12.4	19.5 (P)	+42.8 d (20)	+43
					Found	68.0	12.4	19.7 (P)	+18.8 q (20)	+21

[a] Neo = neopentyl, Ph = phenyl, Vi = vinyl, Me = methyl. [b] For further details of these preparations see the Experimental Section. [c] The listed temperatures are boiling points if they are followed by a pressure in parentheses; otherwise they are melting points. [d] The multiplicities of the proton-decoupled phosphorus-31 resonances are indicated as follows: s = singlet, d = doublet, t = triplet, q = quartet. Figures in parentheses are phosphorus–phosphorus coupling constants in hertz. [e] The additive alkyl group contributions of S. O. Grim, W. McFarlane, and E. F. Davidoff, *J. Org. Chem.*, **32**, 781 (1967), with the additional values (see text) of 6 ppm for the vinyl group and 7 ppm for the PCH$_2$CH$_2$P unit were used for these calculations. [f] The sensitivity of these compounds to aerial oxidation and hydrolyses prevented reliable analytical data from being obtained. The proton, carbon-13, and phosphorus-31 NMR spectra as well as their mass spectra and chemical reactions unambiguously identify these compounds. [g] In view of the fact that neopentyldiphenylphosphine was already reported by S. O. Grim, W. McFarlane, and E. F. Davidoff, *J. Org. Chem.*, **32**, 781 (1967), its analysis was omitted. [h] Literature values from Grim, McFarlane, and Davidoff. [i] These J(P–H) values were obtained from phosphorus-31 NMR spectra taken at 40.5 MHz on a Varian HA-100 spectrometer without proton decoupling.

B. NMR Spectra. The phosphorus-31, proton, and carbon-13 NMR spectra of all of the major new neopentylphosphorus derivatives were taken in order both to confirm their proposed formulas and structures and to establish the spectroscopic properties of neopentyl groups bonded to phosphorus atoms in different environments.

The phosphorus-31 NMR chemical shifts of all of the trivalent neopentylphosphorus derivatives in which the phosphorus atoms are bonded exclusively to carbon atoms can be related to the additive alkyl group contributions to phosphorus-31 NMR chemical shifts of Grim, McFarlane, and Davidoff.[10] In order to test these ideas fully, their values for the alkyl group contributions[12] were supplemented by the value of 6 ppm for the vinyl group contribution obtained by subtracting twice the phenyl group contribution of 3 ppm from the reported[10] phosphorus-31 chemical shift of 12 ppm for diphenylvinylphosphine and the value of 7 ppm for the contribution of a PCH_2CH_2P unit similarly derived from the reported[5] phosphorus-31 NMR chemical shifts of various phenyl poly(tertiary phosphines). In all cases the experimental phosphorus-31 NMR chemical shifts and those calculated from the additive group contributions (Table I) agree within 4 ppm; in most cases the agreement is much better.

The neopentyl methyl protons in all of the neopentylphosphorus derivatives exhibit a singlet around τ 9 in the proton NMR spectrum. The distance of four bonds between the neopentyl methyl protons and phosphorus atoms both makes $|^4J(\text{P–H})|$ negligible and eliminates any significant effects on the chemical shifts of the neopentyl methyl protons arising from changes in the electronic and steric properties of the groups bonded to the phosphorus atom.

The "normal" proton NMR pattern for the neopentyl methylene protons was a doublet with $|^2J(\text{PH})|$ around 4 Hz for trivalent neopentylphosphorus derivatives containing three phosphorus–carbon bonds and around 11 Hz for neopentylphosphine sulfides. This large change in the $|^2J(\text{PH})|$ of the neopentyl methylene protons from neopentylphosphines to the corresponding neopentylphosphine sulfides resembles the similarly large change in the $|^2J(\text{PH})|$ of the methylphosphorus protons from 2–3 Hz in methylphosphines to 12–13 Hz in the corresponding methylphosphine sulfides. In several trivalent neopentylphosphorus derivatives of the type $(Me_3CCH_2)_2PX$ (X = Cl, C_6H_5, and $CH{=}CH_2$) the neopentyl methylene protons exhibit a more complex pattern (Figure 1) which can be interpreted as an AB double doublet with J_{AB} = 14 Hz and with further but unequal couplings of the phosphorus atom to the A and B protons with one of these two $^2J(\text{PH})$ couplings frequently being negligible. The two methylene protons in each of the equivalent neopentyl groups in these $(Me_3CCH_2)_2PX$ derivatives are thus diastereotopic apparently because from the viewpoint of a given neopentyl group the remaining three substituents on the phosphorus atom (a neopentyl group, a lone pair, and the X group) are so nonequivalent that the electron density pattern does not have an effective plane of symmetry bisecting the CH_2 unit of a neopentyl group.[13,14] A completely analogous effect has been previously observed[14] for the isopropyl methyl protons in $C_6H_5P[CH(CH_3)_2]_2$ where the two methyl groups are diastereotopic. A particularly unusual feature of the two diastereotopic methylene protons in a neopentyl group of a $(Me_3CCH_2)_2PX$ derivative is the large difference in the $|^2J(\text{PH})|$ couplings from the phosphorus atom to these two protons.

The proton-decoupled carbon-13 NMR spectra of the neopentyl groups in the neopentylphosphorus derivatives exhibit the expected three doublets from the methylene,

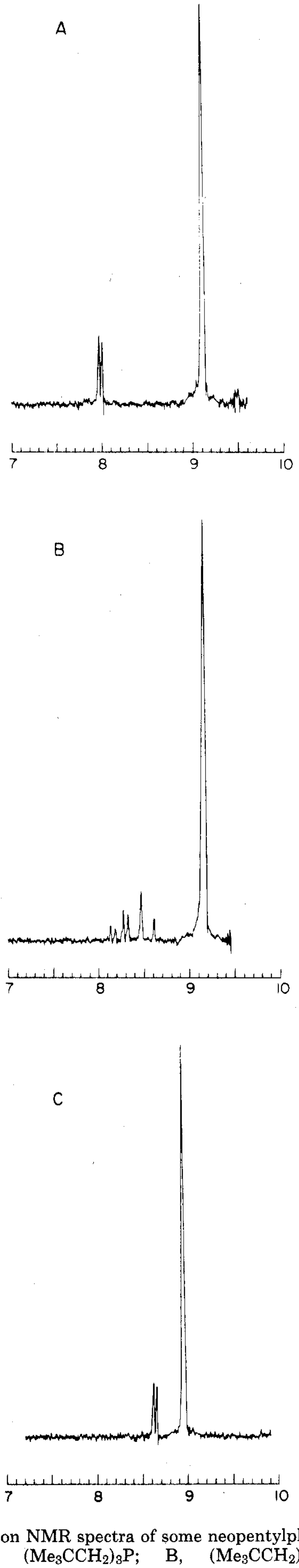

Figure 1. Proton NMR spectra of some neopentylphosphorus derivatives: A, $(Me_3CCH_2)_3P$; B, $(Me_3CCH_2)_2PC_6H_5$; C, $Me_3CCH_2P(C_6H_5)_2$.

quaternary, and methyl carbons each split by coupling with the phosphorus atom. The assignments of the neopentyl carbon resonances appeared obvious on the basis of their relative intensities but nevertheless were checked by off-resonance proton decoupling experiments on $(Me_3CCH_2)_2PH$. The resonances from the methyl and quaternary carbons overlap in the region around δ −31 so that both components of the quaternary carbon doublet could not be clearly separated in all cases. The neopentyl methylene carbon doublet appears in the range δ −37 to −60 and thus could be clearly identified in all compounds.

The carbon–phosphorus coupling constants as observed in the carbon-13 NMR spectrum undergo some interesting changes in going from neopentyl tertiary phosphines to the corresponding phosphine sulfides. The values of the carbon–phosphorus coupling constants in the trivalent neopentylphosphines are similar to the carbon–phosphorus coupling constants found by Mann[15] in the alkyl groups of other alkylphosphines. The $|^1J(CP)|$ from the methylene carbon to the phosphorus atom is 11–15 Hz in the neopentylphosphines but increases to 48–56 Hz in the corresponding neopentylphosphine sulfides. The $|^2J(CP)|$ from the quaternary carbon to the phosphorus atom occurs in a similar range to the $|^1J(CP)|$ (10–16 Hz) in the neopentyl phosphines but decreases to 4–5 Hz in the corresponding neopentylphosphine sulfides. The $|^3J(CP)|$ from the methyl carbons to the phosphorus atom is 9–10 Hz in the neopentylphosphines and decreases slightly to 6–7 Hz in the corresponding neopentylphosphine sulfides. Thus, the effect of sulfurization on the $J(CP)$ coupling constants involving the neopentyl groups in neopentyl phosphines decreases as the distances between the carbon atoms and the phosphorus atom increase although in the trivalent neopentylphosphines the three coupling constants $|^1J(CP)|$, $|^2J(CP)|$, and $|^3J(CP)|$ are rather similar (within a factor of 1.5) despite the different carbon–phosphorus distances.

The carbon-13 resonance from the two equivalent PCH_2CH_2P bridge carbons in the neopentyl di(tertiary phosphine) $(Me_3CCH_2)_2PCH_2CH_2P(CH_2CMe_3)_2$ is a singlet at δ −26.4 similar to the singlets at δ −28.0 and −25.4 reported[16,17] for the PCH_2CH_2P carbons in the related symmetrical di(tertiary phosphines) $R_2PCH_2CH_2PR_2$ (R = methyl and phenyl, respectively). These singlets for the PCH_2CH_2P carbon-13 resonances have been shown[16,17] to be consistent with equal magnitudes but opposite signs for the $^1J(CP)$ and $^2J(CP)$ coupling constants.

Experimental Section

Microanalyses were performed by Atlantic Microanalytical Laboratory, Atlanta, Ga., and Schwarzkopf Microanalytical Laboratory, Woodside, N.Y. Proton NMR spectra (Table II in the microfilm edition) were taken as pure liquids or in $CDCl_3$ solution and recorded at 100 MHz on a Varian HA-100 spectrometer. The phosphorus-31 (Table I) and carbon-13 (Table III in the microfilm edition) NMR spectra were taken using a Jeolco PFT-100 spectrometer operating at 40.3 and 25.03 MHz, respectively, in the Fourier transform mode with proton noise decoupling and a deuterium lock. The phosphorus-31 NMR spectra were taken on the pure liquids or in CH_2Cl_2 solution whereas the carbon-13 NMR spectra were taken in $CDCl_3$ solution unless otherwise indicated. Phosphorus-31 and carbon-13 chemical shifts are reported in parts per million relative to external 85% H_3PO_4 and internal tetramethylsilane, respectively, with positive values indicating upfield chemical shifts. Melting points (Table I) were taken in capillaries and are uncorrected.

Mass spectra of all of the new compounds listed in Table I except for the triphosphine disulfide, the tripod tetraphosphine trisulfide, and the tripod tetraphosphine were taken on the University of Georgia Perkin-Elmer Hitachi RMU-6 mass spectrometer. These mass spectra exhibited molecular ions with the correct *m/e* values as well as ions corresponding to losses of 15 and 56 mass units (CH_3 and C_4H_8, respectively) from the molecular ion. Full details of the fragmentation patterns and associated metastable ions in these 18 mass spectra will be reported elsewhere.

Tetrahydrofuran and dioxane were purified by distillation under nitrogen over sodium benzophenone ketyl immediately before use. Neopentyl chloride was purchased from Columbia Organic Chemicals, Columbia, S.C. Other commercially available starting materials were purchased from normal commercial sources as in previous related papers.[6]

A nitrogen atmosphere was routinely provided for the following three operations: (a) carrying out reactions, (b) handling air-sensitive organophosphorus compounds and the potassium *tert*-butoxide catalyst, and (c) filling evacuated vessels containing potentially air-sensitive materials. A three-necked flask with a fritted disk and stopcock at the bottom was used for filtration of air-sensitive organophosphorus solutions.[18]

Reactions of Neopentylmagnesium Chloride with Phosphorus Trichloride. A. To Give $(Me_3CCH_2)_3P$ and $(Me_3CCH_2)_2P(O)H$. A solution of neopentylmagnesium chloride was prepared from 16 g (0.67 g-atom) of magnesium turnings and 74 ml (64 g, 0.6 mol) of neopentyl chloride in 250 ml of tetrahydrofuran using a small amount of 1,2-dibromoethane to initiate the reaction. This neopentylmagnesium chloride solution was cooled to 0 °C and treated dropwise with 12.6 ml (19.8 g, 0.144 mol) of phosphorus trichloride. The reaction mixture was boiled under reflux for 4.5 h. After stirring overnight at room temperature, the tetrahydrofuran was removed at 25 °C (25 mm) and 200 ml of degassed diethyl ether added. The resulting slurry was cooled to 0 °C and then treated with 250 ml of saturated aqueous ammonium chloride. The ether layer was separated, the aqueous layer was washed three times with diethyl ether, and the combined diethyl ether solutions were dried over anhydrous sodium sulfate. After removal of the diethyl ether from the filtered solutions at 25 °C (25 mm), the liquid residue was distilled under vacuum. Sometimes a small forerun (~1 g) of $(Me_3CCH_2)_2PH$ was obtained; this was spontaneously inflammable in air when absorbed on tissue paper. The major fraction, bp 73–75 °C (0.3 mm), contained a mixture of $(Me_3CCH_2)_3P$ and $(Me_3CCH_2)_2P(O)H$ and solidified readily in the receiver. Fractional crystallization of this solid from ethanol gave $(Me_3CCH_2)_3P$ as the least soluble fraction; an analytical sample, mp 57–59 °C, could be obtained by a second crystallization from hot ethanol. Evaporation of the ethanol from the filtrate after isolating the $(Me_3CCH_2)_3P$ followed by a second vacuum distillation of the residue gave $(Me_3CCH_2)_2P(O)H$, mp 67–69 °C.

B. To Give $(Me_3CCH_2)_2PCl$. A solution of 0.4 mol of neopentylmagnesium chloride in 300 ml of diethyl ether was added dropwise over 2 h to a solution of 14 ml (22 g, 0.16 mol) of phosphorus trichloride in 300 ml of diethyl ether cooled in a 0 °C bath. After stirring overnight at room temperature, the ethereal solution was filtered under nitrogen from the precipitated magnesium salts. The diethyl ether was then removed at 25 °C (25 mm). Vacuum distillation of the residue gave 24.6 g (74% yield) of $(Me_3CCH_2)_2PCl$, bp 49–50 ° (0.4 mm), as the major fraction.

C. To Give $Me_3CCH_2PCl_2$. A solution of 0.3 mol of neopentylmagnesium chloride in 300 ml of diethyl ether was added dropwise over 3 h to a solution of 50 ml (78.5 g, 0.57 mol) of phosphorus trichloride in 500 ml of diethyl ether cooled in a −40 °C bath. After the addition was complete, the reaction mixture was allowed to warm slowly to room temperature. After stirring for 16 h at room temperature, the ethereal solution was filtered under nitrogen pressure. After removal of the diethyl ether at 25 °C (50 mm), vacuum distillation of the liquid residue gave 33–35 g (64–67% yield) of $Me_3CCH_2PCl_2$, bp 76–80 °C (48 mm), as the major fraction.

Preparations of Neopentylphenylphosphines. A tetrahydrofuran solution of neopentylmagnesium chloride was treated dropwise at 0 °C with a solution of the stoichiometric amount of the phenylphosphorus chloride $[C_6H_5PCl_2$ or $(C_6H_5)_2PCl]$ in tetrahydrofuran. After warming to room temperature and boiling briefly under reflux, the tetrahydrofuran was removed at 40 °C (40 mm). Diethyl ether was added to the residue and the mixture hydrolyzed with saturated aqueous ammonium chloride. Distillation of the dried diethyl ether layer gave the neopentylphenyl phosphine as indicated in Table I.

Preparations of Neopentylvinylphosphines. A tetrahydrofuran solution of vinylmagnesium bromide was added dropwise to a solution of the stoichiometric amount of the neopentylphosphorus chloride $[Me_3CCH_2PCl_2$ or $(Me_3CCH_2)_2PCl]$ in tetrahydrofuran at 0 °C. After warming to room temperature and boiling under reflux for 30 min to 2 h the neopentylvinylphosphine (Table I) was isolated by vacuum distillation after aqueous ammonium chloride hydrolysis similar to the isolation of the neopentylphenylphosphines outlined above.

Preparations of Neopentylphosphine Sulfides. Stoichiometric quantities of the tertiary neopentylphosphine and sulfur were boiled under reflux in benzene solution until all of the sulfur dissolved. Solvent was removed from the filtered benzene solution at 25 °C (25 mm). The phosphine sulfides $(Me_3CCH_2)_3PS$ and $(Me_3CCH_2)_2P(S)(C_6H_5)$ were recrystallized from mixtures of dichloromethane and ethanol. The phosphine sulfide $Me_3CCH_2P(S)(C_6H_5)_2$ was crystallized from hot pure ethanol. The phosphine sulfide $(Me_3CCH_2)_2P(S)CH{=}CH_2$ was purified by low-temperature crystallization from hexane. The phosphine sulfide $Me_3CCH_2P(S)(CH{=}CH_2)_2$ was too soluble and low melting to be purified effectively by recrystallization.

Preparation of $(Me_3CCH_2)_2PH$. A solution of 39.5 g (0.19 mol) of $(Me_3CCH_2)_2PCl$ in 100 ml of diethyl ether was added dropwise to 8.0 g (0.21 mol) of $LiAlH_4$ in 200 ml of diethyl ether at −10 °C. The reaction mixture was stirred at room temperature for 24 h and then hydrolyzed at 0 °C by the successive addition of 8 ml of water, 8 ml of 15% aqueous sodium hydroxide, and 24 ml of water. The ether solution was filtered under nitrogen from the precipitated aluminum salts and the diethyl ether removed at 30 °C (30 mm) after drying over anhydrous sodium sulfate. Vacuum distillation of the residue gave 20.9 g (64% yield) of $(Me_3CCH_2)_2PH$, bp 57 °C (5 mm).

Preparation of $Me_3CCH_2PH_2$. A solution of 43 g (0.25 mol) of $Me_3CCH_2PCl_2$ in 200 ml of diethyl ether was added dropwise over 2.5 h to a solution of 15 g (0.4 mol) of $LiAlH_4$ in 500 ml of diethyl ether at −78 °C. The resulting mixture was stirred overnight at room temperature and then hydrolyzed at 0 °C by the successive addition of 15 ml of water, 15 ml of 15% aqueous sodium hydroxide, and 45 ml of water. The diethyl ether solution was filtered under nitrogen from the precipitated solids. After removal of the diethyl ether and all materials boiling below 95 °C by distillation under nitrogen at atmospheric pressure, further atmospheric pressure distillation gave 13.8 g (53% yield) of $Me_3CCH_2PH_2$, bp 95–98 °C (760 mm).

Preparation of $(Me_3CCH_2)_2PCH_2CH_2P(CH_2CMe_3)_2$. A mixture of 8.19 g (0.047 mol) of $(Me_3CCH_2)_2PH$, 9.41 g (0.047 mol) of $(Me_3CCH_2)_2PCH{=}CH_2$, 0.5 g (0.0045 mol) of potassium *tert*-butoxide, and 150 ml of dry toluene was boiled strongly under reflux for at least 24 h. Toluene was then removed at 25 °C (1 mm). Recrystallization of the residue from warm ethanol followed by vacuum sublimation at 80–100 °C (0.1 mm) gave 11 g (63% yield) of $(Me_3CCH_2)_2PCH_2CH_2P(CH_2CMe_3)_2$, mp 66–68 °C.

Preparation of $C_6H_5P(H)CH_2CH_2P(CH_2CMe_3)_2$. A mixture of 4.5 g (0.04 mol) of phenylphosphine,[19] 16.2 g (0.08 mol) of $(Me_3CCH_2)_2PCH{=}CH_2$, sufficient potassium *tert*-butoxide to impart a yellow color (~0.5 g), and 200 ml of tetrahydrofuran was boiled under reflux for a total of 54 h with the addition of sufficient potassium *tert*-butoxide after 18 h to restore the yellow color. Tetrahydrofuran was then removed at 25 °C (25 mm) to leave a residue completely soluble in ethanol. Vacuum distillation of this residue resulted in the recovery of 8.9 g (55% recovery) of $(Me_3CCH_2)_2PCH{=}CH_2$, bp 45 °C (0.7 mm). The residue from this distillation was chromatographed on a degassed Florisil column in hexane solution. The column was eluted with dichloromethane. Testing the eluates with ethanolic nickel(II) chloride gave a red color when elution of the $C_6H_5P(H)CH_2CH_2P(CH_2CMe_3)_2$ began. The product was eluted with dichloromethane and solvent removed from the dichloromethane eluates at 25 °C (25 mm). Vacuum distillation of the resulting thick liquid gave 1.54 g (12.5% conversion, 27% yield) of colorless liquid $C_6H_5P(H)CH_2CH_2P(CH_2CMe_3)_2$, bp 125–140 °C (0.2–0.8 mm), infrared ν(PH) 2285 cm^{-1} (liquid film).

A similar procedure was used to prepare $(Me_3CCH_2)_2PCH_2CH_2P(S)Me_2$ from equimolar quantities of $(Me_3CCH_2)_2PH$ and $Me_2P(S)CH{=}CH_2$ except that the product was isolated by crystallization from a mixture of dichloromethane and hexane rather than by vacuum distillation.

Preparation of $Me_3CCH_2P[CH_2CH_2P(CH_2CMe_3)_2]_2$. A mixture of 20.0 g (0.115 mol) of $(Me_3CCH_2)_2PH$, 10.5 g (0.056 mol) of $Me_3CCH_2P(S)(CH{=}CH_2)_2$, ~1 g of potassium *tert*-butoxide, and 175 ml of tetrahydrofuran was boiled under reflux for 17 h. Solvent was removed at 40 °C (25 mm). The residue was crystallized from ethanol to give 21.2 g of white crystals, apparently impure $Me_3CCH_2P(S)[CH_2CH_2P(CH_2CMe_3)_2]_2$: mp 98–103 °C (unclear), proton-decoupled ^{31}P NMR spectrum δ −47.6 [triplet, J(PP) = 34 Hz] and +42.3 [doublet, J(PP) = 34 Hz]. Anal. Calcd for $C_{29}H_{63}P_3S$: C, 64.9; H, 11.8; S, 6.0. Found: C, 62.0; H, 11.2; S, 8.6. This material was used for the sodium reduction without attempts at further purification.

A mixture of 14.0 g (~0.26 mol) of the crude $Me_3CCH_2P(S)[CH_2CH_2P(CH_2CMe_3)_2]_2$, 2.0 g (0.087 g-atom) of sodium, and 130 ml of dioxane was heated under reflux for 3 h in a 130 °C oil bath. The resulting reaction mixture was filtered first through glass wool and finally through filter paper. Removal of solvent from the filtrate gave 10.9 g [~60% yield based on $Me_3CCH_2P(S)(CH{=}CH_2)_2$] of the tri(tertiary phosphine) $Me_3CCH_2P[CH_2CH_2P(CH_2CMe_3)_2]_2$ as a pale yellow, viscous liquid which could be evaporatively distilled at 170 °C (2 mm).

Attempts to obtain the pure crystalline tri(tertiary phosphine) were unsuccessful. White crystals separated from a methanol solution upon prolonged storage at −15 °C, but these melted upon filtration and warming. Reaction of this neopentyl tri(tertiary phosphine) with ethanolic nickel(II) chloride followed by addition of ethanolic ammonium hexafluorophosphate gave golden yellow needles of the nickel complex [(triphos)NiCl][PF_6]. Anal. Calcd for $C_{29}H_{63}ClF_6NiP_4$: C, 46.8; H, 8.5; Cl, 4.8. Found: C, 46.7; H, 8.6; Cl, 4.8. Degradation of this nickel complex with excess aqueous potassium cyanide followed by addition of dilute aqueous sodium hydroxide regenerated the free $Me_3CCH_2P[CH_2CH_2P(CH_2CMe_3)_2]_2$ as a yellow grease, which still could not be crystallized.

Preparation of $P[CH_2CH_2P(S)(CH_2CMe_3)_2]_3$. A boiling solution of 20.0 g (0.09 mol) of $(Me_3CCH_2)_2P(S)CH{=}CH_2$ in 200 ml of tetrahydrofuran containing 1.5 g (0.013 mol) of potassium *tert*-butoxide was treated with the phosphine gas generated by addition of a solution of 25 ml of water in 75 ml of dioxane to a slurry of 9.2 g (0.16 mol) of aluminum phosphide in 60 ml of dioxane. The gaseous phosphine was dried by passing through two −78 °C traps filled with glass beads before being bubbled below the level of the boiling tetrahydrofuran solution. After all of the phosphine had been added, the reaction mixture was boiled under reflux for an additional 3 h. The reaction mixture became gelatinous upon cooling. Removal of solvent at 30 °C (5 mm) gave 24.6 g (95% yield) of white $P[CH_2CH_2P(S)(CH_2CMe_3)_2]_3$. The analytical sample, mp 237 °C, was obtained by crystallization from a mixture of dichloromethane and hexane.

Preparation of $P[CH_2CH_2P(CH_2CMe_3)_2]_3$. A mixture of 3.0 g (0.0041 mol) of $P[CH_2CH_2P(S)(CH_2CMe_3)_2]_3$, 2.0 g (0.087 g-atom) of sodium metal, and 70 ml of dioxane was heated under reflux for 21 h by a 125 °C oil bath. The reaction mixture became blue after 30 min and milky at the end of the reaction period. The reaction mixture was filtered through glass wool and the dioxane then removed at 25 °C (1 mm). The residue was dissolved in a minimum of hot ethanol and the filtered ethanol solution cooled in a −10 °C freezer for 12 h to give 1.95 g (65% yield) of the crystalline tripod tetra(tertiary phosphine) $P[CH_2CH_2P(CH_2CMe_3)_2]_3$, mp 77–81 °C. This tripod tetra(tertiary phosphine) sublimes slowly at 210 °C (0.5 mm) but this is not recommended as a purification method because of significant decomposition.

Attempts to increase the scale of this reaction resulted in sharply reduced yields.

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Supplementary Material Available. Tables II and III (4 pages). Ordering information is given on any current masthead page.

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Synthesis and Spectral Properties of the Isomeric Hydroxybenzo[*a*]pyrenes

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Syntheses of the 12 isomeric hydroxybenzo[*a*]pyrenes are described. Previous syntheses of eight of these isomers have been repeated and improved upon. New syntheses of the 1-, 2-, 4-, 10-, and 12-hydroxybenzo[*a*]pyrenes are reported. Infrared, ultraviolet, fluorescence, and ^{1}H NMR spectra of the 12 phenols are provided to facilitate study of the metabolism of this important environmental carcinogen.

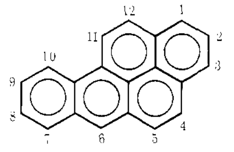
This laboratory has had a long-standing interest in the fundamental mechanisms and pathways through which aromatic compounds undergo oxidative metabolism within the cell.[4] Much of this interest was stimulated by our observation that aromatic ring substituents undergo intramolecular migration and retention (i.e., the NIH shift)[5] during the course of aromatic hydroxylation by monoxygenase enzymes.[6] Occurrence of the NIH shift suggested that aromatic hydroxylation was mediated by arene oxides and led ultimately to the identification of naphthalene 1,2-oxide as the obligatory intermediate in route to the several oxidative metabolites of naphthalene by mammals.[7] The past 5 years have seen a growing interest in the chemistry[8] and biochemistry[9] of arene oxides as this class of compounds has been shown to be potent frameshift mutagens in bacterial test systems, implicated in certain forms of metabolism induced cytotoxicity and necrosis, and shown to induce transformation of mammalian cells in culture (cf. ref 9). Although transformation of cells in culture cannot be directly equated with carcinogenesis in vivo, the possibility does exist that arene oxides are ultimate carcinogens[10] in mammals. For this reason, we have undertaken a comprehensive study of the carcinogen benzo[*a*]pyrene (BP).

Although BP must be classified as a relatively weak carcinogen[11] when compared to 3-methylcholanthrene or 7,12-dimethylbenzo[*a*]anthracene, BP is one of the most prevalent and ubiquitous environmental carcinogens to which man is exposed.[12] In addition, definitive studies of the metabolism of this hydrocarbon should be possible through the use of presently available techniques such as gas chromatography and high-pressure liquid chromatography. Interestingly, BP was the first chemical compound for which a causal relationship with cancer was established.[13]

An initial goal of this program has been the chemical synthesis of primary metabolites, arene oxides and phenols, of BP for use as reference standards in the study of the metabolism of BP. Despite the wide interest in the metabolism and carcinogenicity of this hydrocarbon, the synthesis of only eight of the 12 possible phenols had been described, and none of these were readily available for biological examination. The present study describes synthesis of the unknown phenols of BP and improvements on the prior synthetic procedures. Additionally, spectral and chemical properties of these isomers are reported.

Results and Discussion

From a synthetic standpoint, the hydrocarbon BP can be considered to have four distinct regions into which the hydroxyl group must be introduced: the 1, 2, and 3 positions which are peculiar to pyrene residues in polycyclic aromatic hydrocarbons, the 4,5- and 11,12-K regions, the highly reactive 6 position which can be considered similar to 9,10 (meso) positions in anthracene, and the 7, 8, 9, and 10 positions in the benzo ring. Only two highly selective reactions are known for the parent hydrocarbon, substitution at the 6 position and reaction of the 4,5-K region with osmium tetroxide to form the 4,5-dihydrodiol on hydrolysis of the osmate ester.[14] Thus, the only phenol which has been obtained by direct modification of the parent hydrocarbon is 6-hydroxy BP, which Fieser and Hershberg[15] obtained in good yield by acetoxylation of BP with lead tetracetate.



Synthesis of one of the two possible phenols at each of the K regions has been achieved via intramolecular cyclization of polycyclic hydrocarbon acetic acids in liquid HF to ketones which spontaneously isomerize to phenols. Thus, Fieser and Johnson[16] described the cyclization of 4-chrys-