THE JOURNAL OF Organic Chemistry®

VOLUME 40, NUMBER 10

MAY 16, 1975

Decomposition Reactions of Hydroxyalkylphosphorus Compounds. I. Reaction of Benzylbis(α-hydroxybenzyl)phosphine Oxide with Primary Amines[1a]

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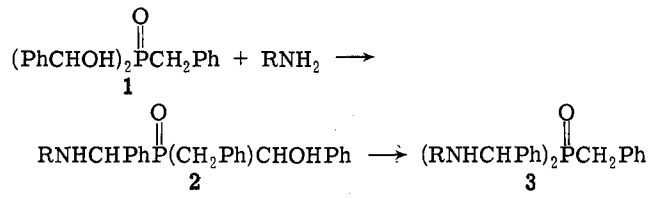
Received November 7, 1974

The reaction of benzylbis(α-hydroxybenzyl)phosphine oxide (1) with primary amines has been shown to produce monomeric, crystalline products in the first example of its kind. Equimolar quantities of 1 and aliphatic primary amines in dilute benzene solutions at reflux afforded the phosphorus amino alcohols, RNHCHPhP(=O)(CH_2Ph)CHOHPh (2). If 2 mol of the amine to 1 mol of 1 were used under these conditions then the diamine, (RNHCHPh)$_2$P(=O)CH_2Ph (3), resulted. Aromatic amines and 1, when combined in equimolar quantities, afforded mixtures of 2 and 3. Aliphatic amines possessing a tertiary carbon adjacent to the nitrogen did not react with 1 under these conditions. The reaction apparently proceeds through decomposition of 1, by loss of 1 mol of benzaldehyde, before reaction with the amine. The loss of benzaldehyde forms a secondary phosphine oxide [PhCHOHP(=O)(H)CH_2Ph] which can add to the imine (formed by reaction of benzaldehyde and the amine) to produce the amino alcohol.

The reaction of hydroxyalkylphosphorus compounds with primary amines has, until recently, afforded only polymeric products.[2-4] Frank, however, demonstrated that the reaction of aniline with tetrakis(hydroxymethyl)-phosphonium chloride or tris(hydroxymethyl)phosphine yields well-defined crystalline monomers.[5] The reaction of bis- or tris(hydroxyalkyl)phosphine oxides with primary or secondary amines has never been shown to yield monomeric products. The aminomethylphosphine oxides have been produced through oxidation of the aminomethylphosphines[6,7] or through addition of a dialkyl phosphite to an imine.[8] Although both tetrakis(hydroxymethyl)phosphonium chloride and tris(hydroxymethyl)phosphine gave good yields of the corresponding aminomethylphosphines when treated with secondary amines,[6,7] tris(hydroxymethyl-)phosphine oxide gave none of the desired aminomethylphosphine oxide when treated with secondary amines under the same conditions.[9] We wish to report the reaction of benzylbis(α-hydroxybenzyl)phosphine oxide (1) with primary amines.

Results and Discussion

The reaction of 1 with primary amines gave 2 or 3 depending on the reaction conditions. This is the first report, to our knowledge, of monomeric products from the reaction of a bis- or trishydroxyalkylphosphine oxide with primary amines. The amino alcohol 2 was produced when equimolar amounts of the primary amine and 1 were heated at reflux in dilute benzene solutions with removal of water by azeotropic distillation into a Dean-Stark trap (method b). By use of very dilute solutions, the reddish color, which often occurs on heating of hydroxyalkylphosphorus compounds, was avoided. Work-up was conducted as described in the Experimental Section and the major product was identified as 2, by NMR, ir, and elemental analysis.



The results of the reaction of 1 with primary amines are summarized in Table I. The NMR spectra of the crude products demonstrated that isomeric mixtures were obtained. Separation of the isomers by fractional recrystallization was not effective in all cases. Only where R = benzyl were two pure isomers isolated. These isomers had visibly different crystalline forms; one formed platelets, 4a, which increased in size on purification by recrystallization (mp 151.5–152.5°), and the other formed needles, 4b (mp 149.5–150.5°). A mixture melting point of 4a and 4b was depressed to 143–148° and the ir and NMR spectra of these stereoisomers were clearly different.

When the carbon adjacent to the amine nitrogen was primary (4, 5, 6, 7, and 8), water evolution was essentially quantitative and the yields of crude product were fair to good. Primary amines bearing secondary alkyl substituents

Table I
Phosphorus Amino Alcohols, RNHCHPhP(=O)(CH_2Ph)CHOHPh

R	Crude yield, %[a]	Recrystallizing solvent	Compd	Mp, °C
$C_6H_5CH_2$	67	Acetone	4a	151.5–152.5
		Methanol	4b	149.5–150.5
$CH_3(CH_2)_7$	54	Ethyl ether–acetone	5	138
$(CH_3)_2CHCH_2$	41	Acetone	6	150–151
$CH_3CH_2CH_2CH_2$	27	Acetone–pentane	7	143–144
$CH_3OCH_2CH_2$	38	Ethyl acetate	8	141–143
c-C_6H_{11}	61	Methanol	9	157.5–159
$(CH_3)_3CCH(CH_3)$	22	Acetone–methanol	10	151–152
c-C_3H_5	32	Methanol–water	11	165–167

[a] Based on the amino alcohol.

(9, 10, and 11) generally gave lower yields of product than the less hindered counterparts with primary alkyl groups, with the exception of cyclohexylamine. This may be indicative of steric requirements of the reaction, since in cyclohexylamine the two carbons β to the nitrogen are tied back into a ring.

The steric requirements of the reaction were further illustrated by the reaction of 1 with amines possessing a tertiary carbon adjacent to the nitrogen. These reactions were unsuccessful. Both *tert*-butylamine and *tert*-octylamine, when combined with 1, were the only treatments with primary amines in which 1 was recovered in sufficient quantities to be identified. The reactions with *tert*-butylamine were run by methods a, b, and c (see Experimental Section) and 1 was recovered in 75, 88, and 77% yields, respectively. The reaction with *tert*-octylamine was run by method b and 1 was recovered in 31% yield. None of the recovered solids from the *tert*-butylamine and *tert*-octylamine reactions with 1 showed any protons between δ 0 and 2 in their NMR spectra, where the terminal methyl group protons would be expected to appear.

Treatment of 1 with primary aromatic amines gave fair to good yields (40–70% based on the amino alcohol) of solid products. Unfortunately, the products were difficult to purify because they decomposed to highly colored materials during recrystallization. The reaction of 1 with aniline or *N,N*-dimethyl-*p*-phenylenediamine gave about equal quantities of the diamine and the amino alcohol after recrystallization. On the other hand, the only product isolated from the reaction of 1 with *p*-nitroaniline was the diamine and the only product isolated from treatment of 1-naphthylamine with 1 was the amino alcohol. The light and/or air sensitivity of these products precluded an accurate material balance, but it is clear that the formation of the diamines is important in the reaction of primary aromatic amines with 1. It remains to be established why the aromatic amines yield the diamines while no diamine was isolated in the aliphatic amine reactions unless 2 mol of the amine were used per mole of 1.

When 2 mol of the amine were used for 1 mol of 1, the diamines 3 were the predominant product. In this manner the benzylamine derivative, 12, was prepared in a 72% yield. A similar reaction, with cyclohexylamine in refluxing toluene, gave the appropriate diamine, 13, in a 39% yield.

In the reactions of benzylamine and octylamine with 1, the last solids collected from the reaction mixture were

$$1 + 2RNH_2 \longrightarrow (RNHCHPh)_2P(=O)CH_2Ph$$

12, R = $PhCH_2$
13, R = C_6H_{11}

higher melting than the earlier fractions. These late fractions were recovered in about 5% yields and identified as the aminobenzylphosphinic acids. The phosphinic acids would arise from the base-catalyzed (or thermally induced) elimination of benzaldehyde from 2 to form the secondary phosphine oxide 16, which would oxidize[10] on standing to form 14 and 15. In all cases, part of the reaction mixture remained as a viscous oil from which no more solid product could be obtained.

$$2 \xrightarrow{RNH_2} RNHCHPhP(=O)(CH_2Ph)CHPh(O^-) \xrightarrow[+H^+]{-PhCHO} RNHCHPhP(=O)(H)CH_2Ph \xrightarrow{[O]} RNHCHPhP(=O)(OH)CH_2Ph$$

16

14, R = $C_6H_5CH_2$
15, R = $CH_3(CH_2)_7$

The reaction of primary amines with 1 could be considered as a nucleophilic displacement of hydroxyl by the amine, which would be unusual. However, since the odor of benzaldehyde was obvious above the reaction mixtures and the aminobenzylphosphinic acids were isolated from the reaction mixture, 1 probably decomposed preceding the reaction with the amine.

A mechanism can be proposed whereby the amine would remove a proton[11,12] from 1 and eliminate benzaldehyde to form 17, which is resonance stabilized by delocalization of the charge to oxygen. The anion removes a proton from the conjugate acid of the amine to form 18. No spectroscopic

$$1 \xrightarrow{RNH_2} PhCHOHP(=O)(CH_2Ph)CHPh(O^-) \xrightarrow{-PhCHO}$$

$$PhCHOHP(=O)CH_2Ph \longleftrightarrow PhCHOHP(O^-)CH_2Ph \quad (17) \xrightarrow{RNH_3^+}$$

$$PhCHOHP(OH)CH_2Ph \rightleftharpoons PhCHOHP(=O)(H)CH_2Ph$$

18 18

evidence indicates the existence of the trivalent form, but kinetic studies show that this species is normally present in extremely low concentrations.[13] For these reasons 18 will be referred to as the "secondary phosphine oxide" with the realization that if the neutral compound is to show nucleophilic reactivity, then the trivalent tautomer of 18 must be the reactive species. The amine could react with the free benzaldehyde to form the imine to which 18 (or its anion 17) would readily add to form the amino alcohol 2.

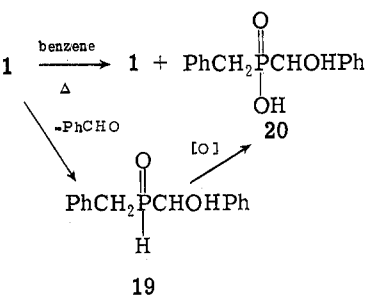
$$RNH_2 + PhCHO \xrightarrow{-H_2O} RN{=}C(Ph)(H) \xrightarrow[\text{or } 17]{18} RNHCHPhP(=O)(CHOHPh)CH_2Ph$$

2

Kreutzkamp and Storck[14] have shown that secondary phosphine oxides will add across the C=N bonds of imines,

isocyanates, etc., to form the tertiary phosphine oxides. Buckler demonstrated that primary phosphine oxides add to the carbonyl group of ketones[15] and that dibenzylphosphine oxide reacts readily with benzaldehyde under acidic conditions[16] to give the tertiary phosphine oxide. Fields has shown that diesters of phosphonic acids react exothermically when mixed with imines.[8] Thus, there is ample precedent for the reaction of a secondary phosphine oxide with an electrophilic center. It is proposed that the reaction occurred through decomposition of 1 to form the secondary phosphine oxide, **18**, which then reacts with the imine, formed from the free benzaldehyde and the amine, to produce the amino alcohol **2**. If this mechanism is operative, then 1 should react with benzaldehyde imines to give similar products. The reaction of 1 with benzaldehyde imines is the subject of an accompanying publication.[17]

The ready decomposition of 1 was further indicated by heating it in refluxing benzene for 4 hr. After removal of the benzene the viscous oil was dissolved in ether and solid slowly precipitated. Eventually 63% of 1 was recovered while another product, identified as benzyl(α-hydroxybenzyl)phosphinic acid (**20**), was isolated in a 12% yield. This product must result from oxidation of the secondary phosphine oxide **18**, which is formed on the loss of benzaldehyde from 1.



Isolation of **20** indicates that decomposition of 1 can occur thermally, without added acid or base.

Experimental Section

Reagent grade chemicals and solvents were used without further purification. Other chemicals and solvents were purified as stated. Benzene, toluene, and xylene were dried for 24 hr or more over Linde molecular sieve 4A before use.

The ir spectra were taken on a Perkin-Elmer Model 137 with NaCl optics. Solid samples were run as KBr pellets using about 1% of the sample. The NMR spectra were taken on a Varian Model A-60A or JeOLCO MH-60-II. Elemental analyses and molecular weight determinations were performed by Enviro Analytical Laboratory, Knoxville, Tenn., and Galbraith Laboratories, Inc., Knoxville, Tenn. All melting points are uncorrected.

Benzylbis(α-hydroxybenzyl)phosphine Oxide (1). Buckler's[16] procedure was used to prepare 1; however, the maximum crude yield was 35%. Recrystallization of the crude product from ethanol gave pure 1, mp 151–52°. The diol was assigned as one of the possible *dl* forms based on its NMR spectrum.[18]

Reaction of Benzylbis(α-hydroxybenzyl)phosphine Oxide (1) with Primary Amines. Method a. When the amine had a sufficiently high boiling point to allow reflux in benzene, the following method was used. Equimolar quantities (5–10 mmol) of 1 and the amine were combined in a boiling flask with 50–60 ml of anhydrous benzene. The flask was fitted with a Dean-Stark trap, a water-cooled condenser, and a drying tube. The contents of the flask were magnetically stirred while being refluxed until water evolution ceased. This was often 6–12 hr after most of the water had evolved to ensure completeness of reaction. The solvent was removed in vacuo, the oily residue was triturated with or dissolved in an appropriate solvent (usually ether, occasionally low-boiling petroleum ether or acetone), and the solid which formed slowly was collected in several fractions over several days to months. This solid was then recrystallized from an appropriate solvent.

Method b. A variation of method a, which often gave better yields of the desired product, consisted of simply using a more dilute solution for reaction. Thus equimolar quantities of 1 and the amine (10–30 mmol) were combined in 500–800 ml of benzene. Reflux was carried out until the water evolution ceased and work-up was carried out as in method a. Although this method often required longer reflux times, the solution would remain water white. In method a the presence of hydroxyalkylphosphorus decomposition products was indicated by the distinct yellow color of the solution after several hours of reflux. In a few cases method b was used with only 1–5 mmol of 1 and the amine in 170–200 ml of benzene.

Method c. Equimolar quantities of 1 and the amine (10–20 mmol) were combined with 600 ml of anhydrous benzene and 40 g of Linde molecular sieve 4A in a 1.5-l. erlenmeyer flask. The flask was stoppered and warmed gently at 30–35° with mechanical shaking for 2 weeks. The reaction mixture was filtered and the solvent was removed in vacuo. The oily residue was triturated with ether, collected, and recrystallized from an appropriate solvent.

Method d. Equimolar quantities of 1 and the amine (5 mmol) were combined with 400 ml of anhydrous benzene and 20 g of Linde molecular sieve 4A in the pressure bomb of a Parr Series 4000 pressure reactor. The bomb was sealed, placed in the heating jacket, and heated at 85° for 6 hr with mechanical agitation. The reaction mixture was cooled and filtered. The solvent was removed in vacuo and the oily residue was triturated with ether. This method was used primarily on gaseous or low-boiling amines.

Benzyl(α-benzylaminobenzyl-α′-hydroxybenzyl)phosphine Oxide (4). The use of method b afforded 67% yield of crude product which was recrystallized three times from acetone to yield white platelets, **4a:** mp 151.5–152.5°; ir (KBr) 3.0 (NH), 3.25 (hydrogen-bonded OH), 3.46 (aliphatic CH), 8.75 μ (P=O); NMR ($CDCl_3$) δ 2.4–3.27 (m, AB portion of an ABX pattern, J_{AB} = 15 Hz, 2 H, PCH_2Ph), 3.61 (q, J = 13 Hz, 2 H, NCH_2Ph), 3.67–4.5 (m, 1 H, NH), 4.08 (d, J = 12 Hz, 1 H, PCHN), 5.36 (d, J = 10 Hz, 1 H, PCHO), 6.67–7.73 (m, 21 H, aromatics plus OH); the multiplet at δ 3.67–4.5 and one of the 21 protons in the aromatic multiplet exchanged with D_2O.

Anal. Calcd for $C_{28}H_{28}NO_2P$: C, 76.17; H, 6.39; N, 3.17; P, 7.02; mol wt, 441.5. Found: C, 76.05; H, 6.34; N, 3.28; P, 7.05; mol wt (MeOH), 432.

The filtrates from the recrystallizations of **4a** were combined and evaporated to dryness in vacuo. The residue was recrystallized four times from methanol to yield white needles, **4b:** mp 149.5–150.5°; ir (KBr) 3.0 (NH, not as sharp as in **4a**), 3.15 and 3.25 (hydrogen-bonded OH), 3.5 (aliphatic CH), 8.70 μ (P=O); NMR ($CDCl_3$) δ 2.37–3.24 (m, AB portion of an ABX pattern, J_{AB} = 15 Hz, 2 H, PCH_2Ph), 3.58 (q, J = 13 Hz, 2 H, NCH_2Ph), 3.16–4.33 (m, 1 H, NH), 4.05 (d, J = 8 Hz, 1 H, PCHN), 5.2 (s, J < 1 Hz, 1 H, PCHO), 6.5–7.57 (m, 21 H, aromatics plus OH); the multiplet at δ 3.16–4.33 and one of the 21 protons in the aromatic multiplet exchanged with D_2O.

Anal. Calcd for $C_{28}H_{28}NO_2P$: C, 76.17; H, 6.39; N, 3.17; P, 7.02. Found: C, 76.12; H, 6.29; N, 3.17; P, 7.10.

Benzyl(α-hydroxybenzyl-α′-octylaminobenzyl)phosphine Oxide (5). The crude yield of product (54%) was obtained by method b. Recrystallization from 150 ml of ethyl ether and 20 ml of acetone yielded the analytical sample, **5:** mp 138°; ir (KBr) 3.0 (shoulder, NH), 3.10 and 3.25 (hydrogen-bonded OH), 3.4 (strong, aliphatic CH), 8.75 and 8.9 μ (P=O); NMR ($CDCl_3$) δ 0.6–1.67 [m, 15 H, $(CH_2)_6CH_3$], 2.0–3.34 (m, 5 H, PCH_2Ph, NCH_2, and NH), 4.07 (d, J = 8 Hz, 0.5 H, PCHN), 4.23 (d, J = 13 Hz, 0.5 H, PCHN), 5.02 (d, J = 8 Hz, 0.5 H, PCHO), 5.23 (s, J < 1 Hz, 0.5 H, PCHO), 6.73–7.63 (m, 16 H, aromatics plus OH); one of the protons under the multiplet at δ 2.0–3.34 and one of the protons under the aromatic multiplet were lost on D_2O exchange. The NMR spectrum clearly shows a mixture of isomers in a 1:1 ratio.

Anal. Calcd for $C_{29}H_{38}NO_2P$: C, 75.10; H, 8.26; N, 3.02; P, 6.68. Found: C, 74.96; H, 8.10; N, 3.06; P, 6.58.

Benzyl(α-hydroxybenzyl-α′-isobutylaminobenzyl)phosphine Oxide (6). A crude yield of 41% was obtained by method b. The white solid was recrystallized three times from acetone to yield long, fluffy needles, **6:** mp 150–151°; ir (KBr) 3.0 (shoulder, NH), 3.15 and 3.25 (hydrogen-bonded OH), 3.36 (aliphatic CH), 8.7 μ (P=O); NMR ($CDCl_3$) δ 0.67–1.03 (m, 6 H, CH_3), 1.33–3.5 (m, 6 H, includes PCH_2Ph, 3.5–2.5, NCH_2, 2.5–2.0, and the NH and $HC(CH_3)_2$ spread over the region), 4.0 (d, J = 8 Hz, 0.625 H, PCHN), 4.15 (d, J = 14 Hz, 0.375 H, PCHN), 4.97 (d, J = 7 Hz, 0.375 H, PCHO), 5.18 (s, J < 1 Hz, 0.625 H, PCHO), 6.67–7.67 (m, 16 H, aromatics plus OH); one of the protons under the multiplet at δ 1.33–3.5 and one of the protons under the aromatic multiplet were lost on D_2O exchange. The NMR spectrum clearly shows a

mixture of isomers with the predominant isomer exhibiting a singlet for the proton on the carbon bonded to both phosphorus and oxygen.

Anal. Calcd for $C_{25}H_{30}NO_2P$: C, 73.69; H, 7.42; N, 3.44; P, 7.60. Found: C, 73.89; H, 7.45; N, 3.26; P, 7.43.

Benzyl(α-butylaminobenzyl-α′-hydroxybenzyl)phosphine Oxide (7). Reaction by method a gave a 27% yield of white solid. Recrystallization from acetone–pentane afforded the analytical sample **7**: mp 143–144°; ir (KBr) 3.0 (shoulder, NH) 3.08, 3.15, 3.25 (hydrogen-bonded OH), 3.39 (aliphatic CH), 8.65 μ (P=O); NMR ($CDCl_3$) δ 0.5–1.71 [m, 7 H, $CH_3(CH_2)_2$], 2.1–2.83 (m, 2 H, NCH_2), 2.83–3.67 (m, 2 H, PCH_2), 3.95 (d, J = 17.5 Hz, 1 H, PCHN), 5.0 (d, J = 11 Hz, 1 H, PCHO), 6.84–7.70 (m, 15 H, aromatics); the NH and OH protons appear to be spread along with the base line at δ 2.0–5.0.

Anal. Calcd for $C_{25}H_{30}NO_2P$: C, 73.69; H, 7.42; N, 3.44; P, 7.60. Found: C, 73.57; H, 7.42; N, 3.37; P, 7.72.

Benzyl[α-hydroxybenzyl-α′-[(2-methoxy)ethylaminobenzyl]]phosphine Oxide (8). A 38% yield of white solid resulted from method b. Recrystallization from ethyl acetate afforded the analytical sample, **8**: mp 141–143°; ir (KBr) 3.0 (shoulder, NH), 3.09 and 3.25 (hydrogen-bonded OH), 8.68 and 8.9 μ (P=O); NMR ($CDCl_3$) δ 2.15–3.67 (m, 9 H, contains PCH_2, NCH_2, CH_3OCH_2, and OCH_3 spike at 3.36), 3.95 (d, J = 18 Hz, 1 H, PCHN), 4.98 (d, J = 12 Hz, 1 H, PCHO), 6.90–7.67 (m, 15 H, aromatics); these assignments were made after D_2O exchange, since the NH and OH protons were spread out along the base line at δ 2.4–5.4. Integration was decreased only in this region after exchange with D_2O.

Anal. Calcd for $C_{24}H_{28}NO_3P$: C, 70.40; H, 6.89; N, 3.42; P, 7.56. Found: C, 70.22; H, 6.76; N, 3.37; P, 7.56.

Benzyl(α-cyclohexylaminobenzyl-α′-hydroxybenzyl)phosphine Oxide (9). From method b the white solid which formed in 58% yield was recrystallized twice from methanol to yield white needles, **9**: mp 157.5–159°; ir (KBr) 3.0 (shoulder, NH), 3.12, 3.17, 3.25 (hydrogen-bonded OH), 3.4 (aliphatic CH), 8.74 μ (P=O); solubility of **9** in $CDCl_3$, DMSO-d_6, and others was too low to obtain an interpretable NMR spectrum.

Anal. Calcd for $C_{27}H_{32}NO_2P$: C, 74.8; H, 7.44; N, 3.23; P, 7.15. Found: C, 74.43; H, 7.47; N, 3.23; P, 7.06.

Benzyl[α-[(3,3-dimethyl)-2-butylaminobenzyl]-α′-hydroxybenzyl]phosphine Oxide (10). Method b produced only a 22% yield of white solid. This was recrystallized twice from acetone–methanol to yield the analytical sample **10**: mp 151–152°; ir (KBr) 3.0 (shoulder, NH), 3.2 (hydrogen bonded OH), 3.38 (aliphatic CH), 8.7 μ (P=O); NMR ($CDCl_3$) δ 0.7–1.17 (m, 12 H, CH_3), 2.02–2.4 (m, 1 H, NCH), 2.5–3.6 (m, 2 H, PCH_2Ph), 4.0–4.5 (m, 1 H, PCHN), 4.8–5.27 (m, 1 H, PCHO), 6.5–7.67 (m, 16 H, aromatics plus OH); the NH proton appears to be spread along the base line at δ 2.0–5.0 and added slightly to the integration of the peaks in this area. The NMR spectrum indicated a complex mixture of isomers despite the narrow melting point range.

Anal. Calcd for $C_{27}H_{34}NO_2P$: C, 74.46; H, 7.87; N, 3.22; P, 7.11. Found: C, 74.49; H, 7.87; N, 3.14; P, 7.18.

Benzyl(α-cyclopropylaminobenzyl-α′-hydroxybenzyl)-phosphine Oxide (11). Reaction by method d gave a 32% yield of white solid which was recrystallized from methanol–water to provide the analytical sample, **11**: mp 165–167°; ir (KBr) 3.0 (NH), 3.17 and 3.22 (hydrogen-bonded OH), 8.71 and 8.86 μ (P=O); NMR (DMSO-d_6), although **11** was not soluble enough to allow for a readily interpretable spectrum, it was possible to show that the aromatic protons and cyclopropyl ring protons were in the proper ratio, δ 0.15–1.23 (m, 4 H, cyclopropyl ring methylene H), 6.7–7.67 (m, 15 H, aromatics).

Anal. Calcd for $C_{24}H_{26}NO_2P$: C, 73.64; H, 6.70; N, 3.58; P, 7.91. Found: C, 73.15; H, 6.75; N, 3.37; P, 8.09.

Benzylbis(α-anilinobenzyl)phosphine Oxide (21). Reaction by method b produced three distinct crystalline fractions on workup (47% yield). The first two were shown to be similar by ir and were combined and recrystallized from toluene to give the analytical sample, **21**: mp 205–207°; ir (KBr) 2.9 and 3.0 (NH), 3.25 (aromatic CH, weak), 6.2 and 6.65 (C=C, very strong), 8.47 and 8.65 μ (P=O); the most intense absorption in the ir spectrum of **21** is the aromatic double bond stretch, which is a sharp contrast from the aliphatic diamines and amino alcohols, where the phosphoryl band is the most intense absorption; NMR ($CDCl_3$) δ 2.0–3.4 (m, 2 H, PCH_2Ph), 5.0 (d, J = 14 Hz, 2 H, PCHN), 6.1–7.67 (m, 25 H, aromatics), these assignments were made on the D_2O-exchanged spectrum since the NH protons were spread along the base line at δ 5.0–2.3 and caused difficulty in the integration.

Anal. Calcd for $C_{33}H_{31}N_2OP$: C, 78.86; H, 6.22; N, 5.57; P, 6.16. Found: C, 78.77; H, 6.08; N, 5.46; P, 6.19.

Benzyl(α-anilinobenzyl-α′-hydroxybenzyl)phosphine Oxide (22). The third crop of solid (10% yield) obtained from the aniline reaction mixture had an ir spectra that was significantly different than the previous two fractions. Recrystallization from methanol gave the analytical sample which was identified as the amino alcohol **22**: mp 171–175°; ir (KBr) 2.95 (NH), 3.15 and 3.25 (hydrogen-bonded OH), 6.25 and 6.67 (intense C=C), 8.7 and 8.9 μ (P=O), as in the dianilino derivative the most intense absorptions in the ir spectrum were the aromatic double bond stretchings; NMR ($CDCl_3$) δ 2.5–3.5 (m, 2 H, PCH_2), 4.2–5.3 (m, 2 H, PCHN, PCHO), 5.9–7.5 (m, 20 H, aromatics), assignments were made on the D_2O-exchanged spectrum as the NH appeared to be spread along the base line at δ 4.0–5.5 while the OH was under the aromatics.

Anal. Calcd for $C_{27}H_{26}NO_2P$: C, 75.86; H, 6.13;N, 3.28; P, 7.25. Found: C, 75.78; H, 6.11; N, 3.29; P, 7.12.

Benzylbis(α-p-nitroanilinobenzyl)phosphine Oxide (23). The use of method b with *p*-nitroaniline produced only the diamine, **23**, in a 47% yield. Attempts at recrystallization yielded lower melting products, so the original material was used as the analytical sample, **23**: mp 195–196°; ir (KBr) 2.95 and 3.05 (NH), 3.25 (medium, aromatic CH), 6.25 (C=C), 6.67 and 7.55 (NO_2), 8.45 (P=O), 9.0 (?), bands at 6.25, 6.67, 7.55, and 9.0 μ are all stronger absorptions than the phosphoryl; NMR (DMSO-d_6) δ 2.9–3.5 (m, 2 H, PCH_2), 5.21 (d, J = 11 Hz, 1 H, PCHN), 5.53 (d, J = 18 Hz, 1 H, PCHN), 6.25–8.0 (m, 23 H, aromatics), the assignments were made on the D_2O-exchanged spectrum as the water present in the DMSO-d_6 interfered with the integration.

Anal. Calcd for $C_{33}H_{29}N_4O_5P$: C, 66.88; H, 4.93; N, 9.46; P, 5.23. Found: C, 67.19; H, 4.98; N, 9.29; P, 5.15.

Benzylbis(α-p-dimethylaminoanilinobenzyl)phosphine Oxide (24). The use of method b with *N,N*-dimethyl-*p*-phenylenediamine produced a mixture of diamine and amino alcohol in a 71% yield. Recrystallization of this solid from acetone–ethanol and twice more from acetone yielded the analytical sample, **24**: mp 173–175°; ir (KBr) 2.85 and 3.02 (NH), 3.28 (aromatic CH), 3.56 (aliphatic CH), 6.57 (C=C), 8.30, 8.58 μ (P=O), the ir identified **24** as the diamine; however, the analysis was off, probably owing to the instability of the compound.

Benzyl(α-p-dimethylaminoanilinobenzyl-α′-hydroxybenzyl)phosphine Oxide (25). The filtrates from above were reduced in volume and recrystallized from methanol–benzene twice to give the analytical sample, **25**: mp 177–179°; ir (KBr) 2.98 (NH), 3.27 (hydrogen-bonded OH), 3.56 (aliphatic CH), 6.57 (C=C), 8.70 μ (P=O). The ir and analysis indicate the amino alcohol.

Anal. Calcd for $C_{29}H_{31}N_2O_2P$: C, 74.0; H, 6.64; N, 5.96; P, 6.58. Found: C, 73.95; H, 6.57; N, 5.93; P, 6.42.

Reaction of 1 with 1-Naphthylamine. Method b produced 3.1 g (73% crude yield) of white to light green solid. Recrystallization of this solid from methanol–benzene mixtures yielded a light beige solid which turned green on standing, **26**: mp 178–180°; ir (KBr) 2.99 (NH), 3.27 (hydrogen-bonded OH), 3.57 (aliphatic CH), 6.60 (aromatic C=C), 8.32 and 8.7 μ (P=O), the ir identified **26** as the amino alcohol, benzyl(α-hydroxybenzyl-α′-1-naphthylaminobenzyl)phosphine oxide, but the analysis was off, probably owing to the instability of **26**.

Reactions of 1 with Methylamine, Ammonia, *tert*-Butylamine, and *tert*-Octylamine. The reactions of **1** with methylamine and ammonia were carried out by method d and both gave highly colored oils from which only very small amounts (0.1–0.25 g) of wide melting point range solids could be isolated. The ir spectra of these solids indicated that they were neither the amino alcohols nor the diamines. The reaction of **1** with *tert*-butylamine was performed by methods a, b, and c. However, the only isolable solid from these reactions was the starting material **1**, which was recovered in 75, 88, and 77% yields, respectively. The reaction of **1** with *tert*-octylamine was carried out by method b but only the starting material (31%) was recovered while the rest of the reaction mixture remained as an intractable oil.

Benzyl(α-benzylaminobenzyl)phosphinic Acid (14). The later fractions collected in the equimolar benzylamine reactions had higher melting points. The ir and NMR spectra of these fractions identified the product as the phosphinic acid **14** (9% yield). Recrystallization from methanol–water yielded the analytical sample, **14**: mp 206–208°; ir (KBr) 2.9 (NH), 3.3 (aromatic CH), 3.4 (aliphatic CH), 3.65–4.5 (hydrogen-bonded POH), 8.33 μ (P=O); NMR ($CDCl_3$) δ 2.64 (d, J = 17 Hz, 2 H, PCH_2), 3.3–4.3 (m, 3 H, includes NCH_2 and PCHN), 6.9–7.7 (m, 15 H, aromatics); assign-

ments were made after D_2O exchange as the NH and POH protons were spread under the spectral region of interest.

Anal. Calcd for $C_{21}H_{22}NO_2P$: C, 71.78; H, 6.31; N, 3.99; P, 8.82. Found: C, 71.95; H, 6.47; N, 3.91; P, 9.08.

Benzyl(α-octylaminobenzyl)phosphinic Acid (15). Similar to the benzylamine reactions, the later solid fractions collected had high melting points. In particular the fourth fraction collected, from the reaction of *n*-octylamine with **1** described above, had mp 182–188° and was recovered in a 4.3% yield. This was recrystallized once from methanol to yield the analytical sample, **15:** mp 193°; ir (KBr) 2.9 (NH), 3.3 (aromatic CH) 3.4 and 3.48 (aliphatic CH), 3.62–4.4 (broad peak, POH), 8.28 μ (P=O).

Anal. Calcd for $C_{22}H_{32}NO_2P$: C, 70.8; H, 8.65; N, 3.76; P, 8.30. Found: C, 70.64; H, 8.53; N, 3.68; P, 8.31.

Benzylbis(α-benzylaminobenzyl)phosphine Oxide (12). A mixture of 3.52 g (0.01 mol) of **1**, 2.14 g (0.02 mol) of benzylamine, and 170 ml of dry benzene was refluxed for 46 hr. Most of the water (0.30 ml, 0.36 ml theoretical) had evolved after 24 hr. The benzene was removed in vacuo and solid formed as the solvent was removed. The oily solid was mixed with ethyl ether and filtered, and 3.8 g (72% yield) of white solid was recovered, mp 135–138°. Two recrystallizations from acetone and one from cyclohexane–$CHCl_3$ gave no improvement in the melting point. However, recrystallization twice from a methanol–water mixture afforded the analytical sample, **12:** mp 144–145°; ir 3.05 (NH), 3.3 (aromatic CH), 3.4 and 3.52 (aliphatic CH), 8.67 μ (P=O); NMR ($CDCl_3$) δ 2.58 (s, 2 H, NH, exchanged with D_2O), 2.68 (d, J = 12 Hz, 2 H, PCH_2Ph), 3.61 (q, J = 13 Hz, 4 H, NCH_2), 4.22 (d, J = 12 Hz, 2 H, PCHN), the simplicity of the NMR spectrum demonstrated that the isomer isolated was the meso form while the NMR of the crude product indicated a mixture of isomers.

Anal. Calcd for $C_{35}H_{35}N_2OP$: C, 79.22; H, 6.65; N, 5.28; P, 5.84. Found: C, 79.32; H, 6.77; N, 5.46; P, 6.01.

Benzylbis(α-cyclohexylaminobenzyl)phosphine Oxide (13). A mixture of 0.99 g (0.01 mol) of cyclohexylamine, 1.76 g (0.005 mol) of **1**, and 50 ml of dry toluene was refluxed for 15 hr. All of the water (0.2 ml, 0.18 ml theoretical) had collected after 4 hr. The solvent was removed in vacuo and the oily residue was dissolved in ether. The solid which precipitated (1.01 g, 39% yield) had mp 133–139°. Recrystallization from methanol–water gave the analytical sample, **13:** mp 139–140°; ir (KBr) 3.0 (NH), 3.25 (aromatic CH), 3.39 and 3.48 (aliphatic CH), 8.55 μ (P=O); NMR ($CDCl_3$) δ 0.6–2.6 (m, 24 H, cyclohexyl ring H, NH), 2.88 (m, 2 H, PCH_2Ph), 4.02 (d, J = 11 Hz, 1 H, PCHN), 4.43 (d, J = 16 Hz, 1 H, PCHN), 6.85–7.5 (m, 15 H, aromatics); after D_2O exchange two protons were lost in the δ 0.6–2.6 region. The complexity of the NMR spectrum demonstrated that the isomer obtained was the *dl* form.

Anal. Calcd for $C_{33}H_{43}N_2OP$: C, 77.01; H, 8.42; N, 5.44; P, 6.02. Found: C, 76.86; H, 8.36; N, 5.21; P, 6.30.

Benzyl(α-hydroxybenzyl)phosphinic Acid (20). A mixture of 10 mmol of **1** and 300 ml of benzene was heated at reflux for 4.5 hr. On cooling, the solution precipitated no solid; so the benzene was removed in vacuo to yield a yellow oil. The oil was triturated with ether overnight to yield 1.26 g (36% recovery) of **1**. Four days later another 0.7 g (20% recovery) of **1** was obtained. Two weeks later another 0.24 g (7%) of **1** was collected while 2 weeks after that a solid was collected which had a ir spectrum markedly different from that of **1**. This solid was identified as benzyl(α-hydroxybenzyl)phosphinic acid (**20**) by NMR and ir spectra and was obtained in an 11.8% yield (0.31 g). The analytical sample was obtained by recrystallization from water–ethanol, **20:** mp 176–177.5°; ir (KBr) 3.0 (OH), 3.25 (aromatic CH), 3.5–5.0 (low broad absorption, POH), 6.7 and 6.9 μ (aromatic C=C); NMR (DMSO-d_6) δ 2.9–3.5 (m, 2 H, PCH_2Ph), 4.89 (d, J = 9 Hz, 1 H, PCHO), 7.03 (broad s, contains COH, POH, and H_2O in DMSO-d_6), 7.1–7.9 (m, 10 H, aromatics).

Anal. Calcd for $C_{14}H_{15}O_3P$: C, 64.12; H, 5.77; P, 11.81. Found: C, 64.10; H, 5.81; P, 11.64.

Registry No.—**1,** 36871-68-8; **4,** 54617-83-3; **5,** 54617-84-4; **6,** 54617-85-5; **7,** 54617-86-6; **8,** 54617-87-7; **9,** 54617-88-8; **10,** 54617-89-9; **11,** 54617-90-2; **12,** 54617-91-3; **13,** 54617-92-4; **14,** 54617-93-5; **15,** 54617-94-6; **20,** 54617-95-7; **21,** 54617-96-8; **22,** 54617-97-9; **23,** 54617-98-0; **24,** 54617-99-1; **25,** 54618-00-7; **26,** 54618-01-8; benzylamine, 100-46-9; octylamine, 111-86-4; isobutylamine, 78-81-9; butylamine, 109-73-9; 2-methoxyethanamine, 109-85-3; cyclohexylamine, 108-91-8; 3,3-dimethyl-2-butanamine, 3850-30-4; cyclopropylamine, 765-30-0; benzenamine, 62-53-3; *p*-nitrobenzenamine, 100-01-6; *N,N*-dimethyl-*p*-phenylenediamine, 99-98-9; 1-naphthylamine, 134-32-7.

References and Notes

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