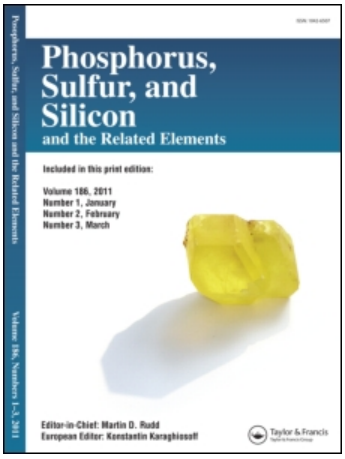

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SYNTHESIS AND PROPERTIES OF TETRAKIS(UREIDOMETHYL)PHOSPHONIUM SALTS

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SYNTHESIS AND PROPERTIES OF TETRAKIS(UREIDOMETHYL)PHOSPHONIUM SALTS

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Hydroxymethylphosphonium salts such as $(HOCH_2)_4PCl$ (**1**), $Ph_3P(CH_2OH)Cl$ (**5**), or $(HOCH_2)_4PI$ (**8**) condense with urea and its methyl derivatives, giving stable ureidomethylphosphonium salts in which the quaternary structure is preserved. With few exceptions, ureas are too feebly basic to cause the dissociation to tertiary phosphine and formaldehyde that characterizes the reactions of hydroxymethylphosphonium salts with primary or secondary amines. The chemistry of the ureidomethylphosphonium salts is explored, particularly with respect to their physical and spectral properties, ion exchange, and hydrolysis with acid or base. If the phosphonium salt contains a hydrogen substituent on N-1, hydrolysis with alkali follows a β-elimination pathway, giving the tertiary phosphine, but if the N-1 position is blocked by a methyl group, the reaction follows the Cahours-Hofmann pathway, giving the tertiary phosphine oxide.

INTRODUCTION

Polymers based on the reaction of tetrakis(hydroxymethyl)phosphonium chloride (**1**) with urea, melamine, and other multifunctional nitrogen compounds are used extensively in flame retardant finishes for cotton.[2] Since **1** is acidic, a base such as triethanolamine or sodium hydroxide is usually added to the formulation to prevent premature polymerization of the reagents. Bases, however, cause **1** to dissociate to tris(hydroxymethyl)phosphine and formaldehyde, resulting in polymers that have a tertiary phosphine structure rather than a quaternary phosphonium salt structure.[3] A notable exception is the Proban[4] finish, in which **1** is condensed with urea in a 2:1 ratio in the absence of base to form a stable, water-soluble precondensate that is subsequently polymerized with ammonia.[5,6] In this paper, we report our investigation of the reaction of **1** with urea or substituted ureas to displace all four of the hydroxyl groups, resulting in a series of novel ureidomethylphosphonium salts in which the quaternary structure is preserved. The chemistry of the phosphonium salts is explored, particularly with respect to their physical and spectral properties, ion exchange, acid hydrolysis, and conversion to tertiary phosphines or their oxides by base.

RESULTS AND DISCUSSION

Phosphonium Chlorides

Condensation of the phosphonium chloride **1** with the ureas **2a–e** took place in refluxing toluene, with azeotropic removal of the water, giving tetrakis(ureidomethyl)phosphonium chlorides (**3a–e**) in good yield (Eq. 1).[7,8]

$$\underset{\mathbf{1}}{(HOCH_2)_4PCl} + 4\,\underset{\mathbf{2}}{R_1R_2NCONHR_3} \rightarrow \underset{\mathbf{3}}{[R_1R_2NCON(R_3)CH_2]_4PCl} + 4\,H_2O \qquad (1)$$

a, $R_1 = R_2 = R_3 = H$
b, $R_1 = CH_3$, $R_2 = R_3 = H$
c, $R_1 = R_2 = CH_3$, $R_3 = H$
d, $R_1 = R_3 = CH_3$, $R_2 = H$
e, $R_1, R_3 = (CH_2)_2$, $R_2 = H$

The 1,3-dimethylurea derivative **3d** crystallized during the condensation and was purified by recrystallization. The cyclic urea derivative **3e** was isolated as a white solid. The others were isolated as viscous, colorless oils. Efforts to purify them by adsorption on a cation exchange resin followed by displacement with hydrogen chloride, as described elsewhere for the carbamate derivatives of **1**,[9] were complicated by the tendency of the ureido nitrogens to form salts with the hydrogen chloride.

The products **3a–e** are air-stable, odorless compounds that, unlike **1**, are neutral in aqueous solution. Their infrared spectra display strong, sharp absorption bands in the 1625 cm^{-1} (C=O, amide I) and 1540 cm^{-1} (N–H, amide II) regions characteristic of the alkylureas.[10] The urea derivative **3a** also shows a strong, sharp band in the 1680 cm^{-1} (NH_2, amide II) region, characteristic of the monoalkylureas.[10]

The ^1H and ^{31}P nmr spectra of **3a–d** are consistent with their formulation as phosphonium salts that have four identical ureido substituents. Each compound shows a single peak in the ^{31}P spectrum in the 26.4 to 32.0 ppm range and a doublet in the ^1H spectrum in the 3.75 to 4.75 ppm range, owing to coupling of the CH_2 protons with phosphorus ($^2J_{PH}$ = 4.0 Hz). The N-3 methyl protons appear at 2.63 to 2.72 ppm in the ^1H spectra of **3b-d**, and are coupled with the NH proton ($^3J_{HH}$ = 4.0 Hz) in **3b** and **3d**. The N-1 methyl protons in the spectrum of **3d** appear further downfield at 2.98 ppm, and are coupled with phosphorus ($^4J_{PH}$ = 2.0 Hz).

The reaction of **1** with 1,1,3-trimethylurea (**2f**) in toluene gave the theoretical amount of water, but over half of the chlorine (55.9%) ended up in a degradation product identified as the trihydrochloride salt of tris(dimethylaminomethyl)phosphine.[11] The base strength of the urea, which increased with each methyl substituent, had evidently reached the point where it interfered with the condensation. Under milder conditions, with benzene as the azeotroping solvent, reaction ceased when 3 moles of water had been displaced, giving (hydroxymethyl)tris(1,3,3-trimethylureidomethyl)-phosphonium chloride (**4f**) as a white, crystalline solid in 61.1% yield (Eq. 2).

$$\underset{1}{} + 3\underset{2}{R_1R_2NCONHR_3} \rightarrow \underset{4}{(HOCH_2)(R_1R_2NCONR_3CH_2)_3PCl} + 3H_2O \qquad (2)$$

f, $R_1 = R_2 = R_3 = CH_3$

Thiourea and 1,3-diethylthiourea both reacted incompletely with **1**, giving 70% and 39%, respectively, of the calculated amount of water. The products were malodorous, glassy substances. Alloxan hydrate and 1,3-diphenylurea both failed to react with **1** in toluene, and decomposed in xylene. 4,5-Dihydroxy-2-imidazolidinone[12] decomposed when heated with **1** in toluene, giving a black, tarry mass.

In some cases, the condensation of **1** with ureas could be carried out in the presence of water, omitting the azeotropic distillation. The reaction with urea, for example, was unaffected by this change, but 1,3-dimethylurea gave only 25.0% of **3d**; the remainder, a heavy oil, could not be induced to yield any more water or **3d** even when subjected to azeotropic distillation with toluene and more 1,3-dimethylurea.

Condensation of (hydroxymethyl)triphenylphosphonium chloride (**5**) with 1,3-dimethylurea in toluene, under the conditions employed with **1**, produced only triphenylphosphine (88.2%). Under milder conditions, with benzene as the azeotroping solvent, the yield of triphenylphosphine dropped to 22.5% and the desired product, (1,3-dimethylureidomethyl)triphenylphosphonium chloride (**6d**), was obtained in 75.7% yield. Condensation of **5** with urea or 1,1-dimethylurea in benzene gave the phosphonium salts **6a** and **6c** in good yield, without side reactions (Eq. 3).

$$\underset{5}{Ph_3P(CH_2OH)Cl} + \underset{2}{R_1R_2NCONHR_3} \rightarrow \underset{6}{Ph_3P(CH_2NR_3CONR_1R_2)Cl} + H_2O \qquad (3)$$

The dimethylurea derivatives **6c** and **6d** were both crystalline solids. Their ^1H nmr spectra exhibit no coupling between CH_2 and P, nor the long-range coupling between NH and aromatic protons previously encountered in **5** and its methyl carbamate derivative $Ph_3P(CH_2NHCO_2CH_3)Cl$ (**7a**).[9] Peterson and Reuther prepared **6c**, mp 205°d., in 64% yield by the reaction of triphenylphosphine with 3,3-dimethyl-1-(methoxymethyl)urea and hydrogen chloride in methanol,[13] and also used this method to prepare the bromide analog of **6d**, mp 210–214°d., in 66.5% yield.[14]

Other Phosphonium Salts

The chloride ion in the phosphonium chlorides can be replaced by other anions such as bromide, iodide, picrate, etc. The phosphonium iodide **9d** was prepared either by condensing tetrakis(hydroxymethyl)phosphonium iodide (**8**) with 1,3-dimethylurea,[15] or by metathesis of the phosphonium chloride **3d** with sodium iodide:

$$\begin{array}{ccc} \underset{1}{(HOCH_2)_4PCl} & \xrightarrow{2d} & \underset{3d}{[CH_3NHCON(CH_3)CH_2]_4PCl} \\ \downarrow \text{NaI} & & \downarrow \text{NaI} \\ \underset{8}{(HOCH_2)_4PI} & \xrightarrow{2d} & \underset{9d}{[CH_3NHCON(CH_3)CH_2]_4PI} \end{array}$$

Reaction of **3d** with picric acid in water, following Schindlbauer's procedure,[16] gave a bright yellow, chloride-free product identified by elemental analysis as the phosphonium hydrogen dipicrate (**10d**). The second picric acid moiety was probably a salt of one of the ureido nitrogens.

Acid Hydrolysis

Hydrolysis of the phosphonium salt **3d** with 6*N* hydrochloric acid at 110° cleaved off two of the eight N-methyl groups as methylamine hydrochloride. No trace was found of **1** (or its by-product), the major product of the acid hydrolysis of the carbamate derivatives of 1.[9]

Alkaline Hydrolysis

Hydrolysis of the phosphonium salts **3a–c** with aqueous sodium hydroxide under ambient conditions resulted in an exothermic reaction, giving the tertiary phosphines **11a–c** (Eq. 4).

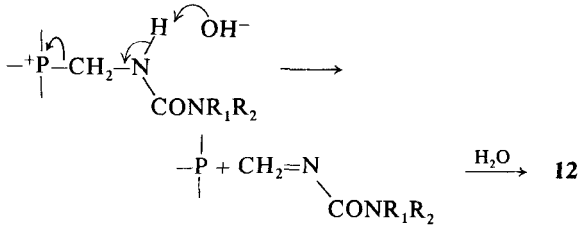
$$\mathbf{3} + NaOH \rightarrow \underset{\mathbf{11}}{(R_1R_2NCONHCH_2)_3P} + \underset{\mathbf{12}}{R_1R_2NCONHCH_2OH} + NaCl \quad (4)$$

The phosphonium salts **3a–c** were unaffected by ammonium hydroxide. Clearly, these salts are more resistant to hydrolysis than the carbamate derivatives,[9] not only to acid but also to base.

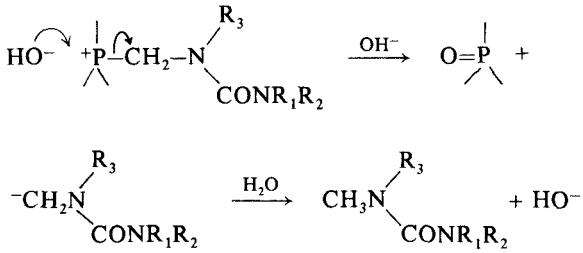
Hydrolysis of the phosphonium salt **3d** with sodium hydroxide, however, gave the tertiary phosphine oxide **13d** directly, in almost quantitative yield (98.5%). The by-product was isolated and identified as 1,1,3-trimethylurea (95.7%) (Eq. 5).

$$\mathbf{3d} + NaOH \rightarrow \underset{\mathbf{13d}}{[CH_3NHCON(CH_3)CH_2]_3PO} + \underset{\mathbf{2f}}{CH_3NHCON(CH_3)_2} + NaCl \quad (5)$$

In this case, the reaction followed the classic Cahours-Hofmann pathway taken by the majority of phosphonium salts,[17, 18b, 19] rather than the tertiary phosphine elimination pathway taken by α-hydroxyalkylphosphonium salts,[18a, 20] the few α-aminoalkylphosphonium salts that we have prepared to date,[9, 21] and a few other specific cases.[20] The reason for the change is undoubtedly the blocking of the N-1 nitrogen in **3d** by the methyl group R_3. If $R_3 = H$, the preferred pathway is attack of hydroxide ion on N–H, followed by β-elimination of the tertiary phosphine:



If $R_3 = CH_3$, however, the hydroxide ion is forced to attack the phosphorus, displacing a ureidomethyl anion:



To confirm this hypothesis, the hydrolysis experiments were focused on the triphenylphosphonium salts **5**, **6** and **7**, whose displacement products, triphenylphosphine or its oxide, are both well-known, stable compounds (Table I).

TABLE I

Alkaline hydrolysis of phosphonium salts

$$[Ph_3PY]Cl + NaOH \rightarrow \begin{Bmatrix} Ph_3P + YOH \\ Ph_3PO + YH \end{Bmatrix} + NaCl$$

Phosphonium Salt	Y	Ph_3P % Yield	Ph_3PO % Yield
5	CH_2OH	95	0
6a	$CH_2NHCONH_2$	81	0
6c	$CH_2NHCON(CH_3)_2$	98[a]	0
6d	$CH_2N(CH_3)CONHCH_3$	8	85[b]
7a[9]	$CH_2NHCO_2CH_3$	81	1

By-products: (a) 1,1-Dimethylurea (81%). (b) 1,1,3-Trimethylurea (87%).

The urea and 1,1-dimethylurea derivatives **6a** and **6c** both gave oxide-free triphenylphosphine in quantitative yield, whereas the 1,3-dimethylurea derivative **6d** gave a mixture of triphenylphosphine (8%) and triphenylphosphine oxide (85%). The by-products from **6c** and **6d** were isolated and identified as 1,1-dimethylurea (81%) and 1,1,3-trimethylurea (87%), respectively. The hydroxymethyltriphenylphosphonium salt **5** gave triphenylphosphine exclusively, as reported by Hoffmann.[22] The methyl carbamate derivative **7a**, included for comparison, gave triphenylphosphine (81%) and triphenylphosphine oxide (1%).

The evidence supports the hypothesis that the nature of the substituent R_3 determines the major pathway of alkaline hydrolysis, though not the exclusive pathway.

Incidentals

Other compounds synthesized in the course of this work included 1-(hydroxymethyl)-1,3-dimethylurea

(**12d**), methylenebis(1,3-dimethylurea) (**14d**), tetrakis(hydroxymethyl)phosphonium iodide (**8**), and 1,1,3-trimethylurea (**2f**).

EXPERIMENTAL[23]

Tetrakis(1,3-dimethylureidomethyl)phosphonium Chloride (**3d**). *A. From Crystalline* **1**. A mixture of the phosphonium chloride **1** (9.53 g, 0.05 mol), 1,3-dimethylurea (17.62 g, 0.20 mol), and toluene (75 ml) was heated to reflux in an apparatus fitted with a Dean-Stark trap for azeotropic removal of the water. The mixture was held at reflux until the evolution of water ceased; 3.7 ml (0.20 mol) was collected in 1 h, and no more passed over in the next hour. The product, which had separated during the reaction as a mass of white solids, was broken up, triturated under toluene, filtered, and dried, giving 22.88 g (97.2%) of **3d** as a white, crystalline solid, mp 187–189°d. Two recrystallizations from 2-propanol (8 ml/g), followed by drying under vacuum for 2 h at 56° (acetone), gave a 1:1 solvate of **3d** and 2-propanol, mp 194–194.5°d; ir (Nujol) 950 (w) cm^{-1}; ^1H nmr (dmso-d_6) δ 1.06 (d, 6H, CH_3, $J = 6.0$ Hz).

Anal. Calcd for $C_{19}H_{44}ClN_8O_5P$: C, 42.84; H, 8.09; Cl, 6.86; N, 20.95; P, 5.84. Found: C, 42.97; H, 8.35; Cl, 6.68; N, 21.11; P, 5.83.

Further drying under vacuum for 4 h at 100° (water) gave pure **3d** as a white, crystalline solid, mp 194–194.5°d; ir (Nujol) 1540 (vs, NH, amide II), 1630 and 1650 (s and vs, C=O, amide I), and 3300 (m, NH) cm^{-1}; ^1H nmr (dmso-d_6) δ 2.63 (d, 12H, and 2-propanol, mp 194–194.5° a; ir (Nujol) 950 (w) cm^{-1}; ^1H 12H, 1-CH_3, $J = 2.0$ Hz), 3.77 (d, 8H, CH_2, $J = 4.0$ Hz), and 7.02 (d, 4H, NH, $J = 4.0$ Hz, vanishing with D_2O); ^{31}P nmr (H_2O) δ 32.0.

Anal. Calcd for $C_{16}H_{36}ClN_8O_4P$: C, 40.63; H, 7.83; Cl, 7.73; N, 23.62; P, 6.75; mol wt, 471. Found: C, 40.80; H, 7.71; Cl, 7.53; N, 23.80; P, 6.58; mol wt (osmometric in H_2O), 274, 286.[24]

The phosphonium salt **3d** is soluble in water, the lower alcohols, and dimethylsulfoxide, and insoluble in other common organic solvents. The solvate is not formed when **3d** is just rinsed or rubbed with 2-propanol.

B. From Aqueous **1**. For large-scale preparations, it is more convenient to add **1** in the form of its commercially available 80% aqueous solution,[25] drop by drop to a preheated solution of 1,3-dimethylurea in toluene and remove the water by azeotropic distillation as reaction proceeds. On a 2.5 mol scale, the yield of **3d**, mp 191–192°d, was 921 g (78.2%).

Tetrakis(ureidomethyl)phosphonium Chloride (**3a**). *In Toluene.* Reaction of **1** (9.53 g, 0.05 mol) with urea (12.01 g, 0.20 mol) in toluene (75 ml), following Procedure A, yielded 3.3 ml (0.18 mol) of water and 18.14 g (101%) of **3a** as a colorless, brittle glass; ir (dmso) 1540 (s, NH, amide II), 1625 (m, C=O, amide I), 1680 (vs, NH_2, amide II), and 3350 (s, NH) cm^{-1}; ^1H nmr (D_2O) δ 4.25 (d, CH_2, $J = 4.0$ Hz); ^{31}P nmr (H_2O) δ 29.5. The phosphonium salt **3a** is soluble in water (pH 6.9) and dimethylsulfoxide, and insoluble in any of the common organic solvents.

The product, dissolved in water (25 ml), was passed onto a cation exchange resin,[9] rinsed with water until chloride-free, and then displaced with 6*N* HCl, giving 11.21 g (44.5%) of the solid trihydrochloride dihydrate; ir (KBr) as above.

Anal. Calcd for $C_{18}H_{27}Cl_4N_8O_6P$: Cl, 28.13; N, 22.23; P, 6.14. Found: Cl, 28.12; N, 22.03; P, 5.79.

In Water. A mixture of 80% **1**[25] (23.82 g, 0.10 mol) and urea (24.02 g, 0.40 mol) was heated to reflux in an oil bath. The urea dissolved at 100°, giving a clear, colorless solution. After 30 min[26] at reflux, the solution was cooled, stripped in a rotary evaporator, and dried over phosphorus pentoxide, giving 36.18 g (100.8%) of **3a** as a colorless, brittle glass; ^{31}P nmr (H_2O) δ 29.5.

Tetrakis(3-methylureidomethyl)phosphonium Chloride (**3b**). Reaction of **1** (9.53 g, 0.05 mol) with methylurea (14.82 g, 0.20 mol) in toluene (75 ml), following Procedure A, yielded 3.0 ml (0.17 mol) of water and 20.78 g (100%) of **3b** as a brittle amber glass; ^1H nmr (D_2O) δ 2.68 (s, 12H, CH_3), 4.25 (d, 8H, CH_2, $J = 4.0$ Hz), and other peaks in the 2.8 to 4.7 region; ^{31}P nmr (H_2O) δ 28.5. The phosphonium salt **3b** is soluble in water (pH ~ 7), ethanol and dimethylsulfoxide, and insoluble in ether, chloroform, benzene, and ethyl acetate.

The product, dissolved in water (30 ml), was passed onto the cation exchange resin,[9] rinsed with water until chloride-free, and then displaced with 6*N* HCl, giving 25.52 g (88.3%) of the liquid trihydrochloride trihydrate, $n^{20}D$ 1.5474; ir (neat) 1560 (s, NH, amide II), 1640 (s, C=O, amide I), and 3330 (s, NH cm^{-1}).

Anal. Calcd for $C_{12}H_{37}Cl_4N_8O_7P$; Cl, 24.52; N, 19.38; P, 5.36. Found: Cl, 22.23; N, 19.07; P, 5.64.

Tetrakis(3,3-dimethylureidomethyl)phosphonium Chloride (**3c**). Reaction of **1** (9.53 g, 0.05 mol) with 1,1-dimethylurea (17.62 g, 0.20 mol) in toluene (75 ml), following Procedure A, gave 3.6 ml (0.20 mol) of water and 23.47 g (99.7%) of **3c** as a colorless, hygroscopic resin; ir (neat) 1530 (vs, NH, amide II), 1645 (vs, C=O, amide I) and 3300 (m, NH) cm^{-1}; ^1H nmr (D_2O) δ 2.96 (s, 24H, CH_3) and 4.30 (d, 8H, CH_2, $J = 3.5$ Hz); ^{31}P nmr (H_2O), δ 26.4.

Tetrakis[(2-oxo-1-imidazolidinyl)methyl]phosphonium Chloride (**3e**). Reaction of **1** (9.53 g, 0.05 mol) with 2-imidazolidinone (17.22 g, 0.20 mol) in toluene (75 ml), following Procedure A, gave 4.1 ml (0.23 mol) of water and 22.23 g (96.1%) of **3e** as a white solid, mp 220°. The product was soluble in dilute NaOH, and insoluble in water or organic solvents.

(Hydroxymethyl)tris(1,3,3-trimethylureidomethyl)phosphonium Chloride (**4f**). Reaction of **1** (9.53 g, 0.05 mol) with 1,1,3-trimethylurea[27] (20.43 g, 0.20 mol) in benzene (75 ml), following Procedure A, gave 3.0 ml (0.17 mol) of water and 25.54 g of oil that partly crystallized on standing. The semisolid mass was rubbed with ethyl acetate and filtered, giving 13.53 g (61.1%) of **4f** as a white, crystalline solid, mp 151–152°d. after recrystallization from acetone (20 ml/g); ir (Nujol) 1600 (vs, C=O, amide I) cm^{-1}; ^1H nmr ($CDCl_3$) δ 2.88 (s, 18H, 3-CH_3), 3.17 (d, 9H, 1-CH_3, $J = 1.5$ Hz), 4.13 (d, 6H, PCH_2N, $J = 4.0$ Hz), and 4.46 (br s, 2H, PCH_2O).

Anal. Calcd for $C_{16}H_{36}ClN_6O_4P$: C, 43.38; H, 8.19; Cl, 8.00; N, 18.98; P, 6.99. Found: C, 43.78; H, 8.60; Cl, 7.99; N, 19.04; P, 7.12.

The phosphonium salt **4f** is soluble in water, chloroform, and acetonitrile, and insoluble in ethyl acetate, carbon tetrachloride, 2-propanol, and cyclohexane.

(1,3-Dimethylureidomethyl)triphenylphosphonium Chloride (**6d**). Reaction of **5**[28] (3.29 g, 0.01 mol) with 1,3-dimethylurea (0.88 g, 0.01 mol) in benzene (25 ml), following Procedure A, gave 3.02 g (75.7%) of **6d** as a white, crystalline solid, mp 191–193°d. One recrystallization from 2-propanol (7 ml/g), followed by thorough drying under vacuum at 100°, gave pure **6d**, mp

195–196°d.; ir (Nujol) 1545 (s, NH, amide II), 1585 (w, C=C), 1650 (vs, C=O, amide I), and 3240 (s, NH) cm^{-1}; ^1H nmr ($CDCl_3$) δ 2.48 (s, 3H, 3-CH_3), 3.10 (d, 3H, 1-CH_3, J = 1.0 Hz), 5.74 (s, 2H, CH_2), and 7.83 (m, 15.5H, C_6H_5 and NH, unchanged by D_2O); ^{31}P nmr ($CHCl_3$), δ 17.0.

Anal. Calcd for $C_{22}H_{24}ClN_2OP$: C, 66.24; H, 6.06; Cl 8.89; N, 7.03; P, 7.76. Found: C, 66.35; H, 6.10; Cl, 9.11; N, 7.10; P, 7.85.

The phosphonium salt **6d** is soluble in water, ethanol, and chloroform, and insoluble in acetone, ether, benzene, and carbon tetrachloride. Like **3d**, the recrystallized solid retains solvent tenaciously.

The filtrate from the main reaction, stripped of benzene, stirred with water, and filtered, yielded 0.59 g (22.5%) of triphenylphosphine, mp 78–79° (ir).

(3,3-Dimethylureidomethyl)triphenylphosphonium Chloride (**6c**). The reaction of **5**[28] (3.29 g; 0.01 mol) with 1,1-dimethylurea (0.88 g, 0.01 mol) in benzene (25 ml), following Procedure A, gave 3.72 g (93.2%) of **6c** as white, crystalline solid, mp 202–203°d. One recrystallization from acetonitrile (25 ml/g) gave pure **6c**, mp 205–206°d. (lit.[13] mp 205°d.); ir (Nujol) 1500 (vs, NH, amide II), 1550 (m, C=C), 1620 (vs, C=O, amide I) and 3000 (s, NH) cm^{-1}; ^1H nmr ($CDCl_3$) δ 2.80 (s, 6H, CH_3), 5.28 (d, 2H, CH_2, J = 6.0 Hz, collapsing with D_2O to s), ~8.0 (m, 15H, C_6H_5), and ~8.8 (m, 1H, NH, vanishing with D_2O); ^{31}P nmr (ethanol) δ 19.9.

The solubility characteristics of **6c** and **6d** are similar, but the former is more soluble in 2-propanol.

Tetrakis(hydroxymethyl)phosphonium Iodide (**8**). A slurry of **1** (47.64 g, 0.25 mol) in ethanol (100 ml) was mixed with a solution of sodium iodide (37.47 g, 0.25 mol) in ethanol (100 ml), stirred 2 h, filtered, concentrated to low volume, filtered again, and stripped in a rotary evaporator, giving 68.34 g (96.9%) of **8** as a pale yellow oil. The oil was covered with benzene and dried by azeotropic distillation from an oil bath, with efficient stirring to prevent overheating. The product was a pale yellow, malodorous oil, n_D^{20} 1.5948; ir (neat) 865 (m, br), 917 (m), 1035 (vs, CO), 1090 (m), 1175 (m), 1290 (m), 1370 (m), 1410 (m), 1545 (w), 1630 (w), 2080 (w), 2570 (w), 2920 (m), and 3330 (vs, OH) cm^{-1}; ^1H nmr (D_2O) δ 4.78 (d, CH_2, J = ~2 Hz); ^{31}P nmr (H_2O) δ 26.5 (m, J_{PCH} = 1.7 Hz; six of the nine lines were discernible after tenfold expansion).

Tetrakis(1,3-dimethylureidomethyl)phosphonium Iodide (**9d**). *From* **8**. Reaction of **8** (7.05 g, 0.025 mol) with 1,3-dimethylurea (8.81 g, 0.10 mol) in toluene (25 ml), following Procedure A, gave 13.65 g (97.1%) of **9d** as a white, crystalline solid, mp 194°d. after two recrystallizations from ethanol (10 ml/g); ir (Nujol) 1530 (vs, br, NH, amide II), 1640 (vs, C=O, amide I), and 3330 (s, NH) cm^{-1}; ^1H nmr (dmso-d_6) δ 2.63 (d, 12H, 3-CH_3, J = 4.0 Hz, collapsing with D_2O to s, δ 2.65), 2.97 (d, 12H, 1-CH_3, J = 1.0 Hz), 3.76 (d, 8H, CH_2, J = 4.0 Hz), and 6.78 (d, 4H, NH, J = 4.0 Hz, vanishing with D_2O); ^{31}P nmr (H_2O) δ 31.5.

Anal. Calcd for $C_{16}H_{36}IN_8O_4P$: C, 34.17; H, 6.45; I, 22.56; N, 19.93; P, 5.51. Found: C, 34.17; H, 6.35; I, 22.79; N, 19.81; P, 5.56.

From **3d**. A solution of sodium iodide (3.00 g, 0.02 mol) in ethanol (80 ml) was treated with **3d** (9.42 g, 0.02 mol) in small portions, stirred 2 h at room temperature, heated to boiling, filtered hot to remove the sodium chloride (0.83 g, 70.9%, giving a negative test for iodide with acidified iodate), concentrated to small volume, and filtered again, giving 9.03 g (80.3%) of **9d** as a white, crystalline solid, mp 193–194°d. One recrystallization from ethanol gave pure **9d**, indistinguishable from the product above by mp, ir, or ^1H nmr.

Anal. Calcd for $C_{16}H_{36}IN_8O_4P$: I, 22.56; P, 5.51. Found: I, 22.78; P, 5.56.

Neither product suffered any weight loss when dried under vacuum for 2 h at 100°.

Tetrakis(1,3-dimethylureidomethyl)phosphonium Hydrogen Dipicrate (**10d**). Picric acid (0.69 g, 3.0 mmol) was added to a solution of **3d** (1.41 g, 3.0 mmol) in water (15 ml), heated to boiling, and allowed to cool. The product (1.01 g, 72.5%) separated as a mass of bright yellow crystals, mp 101–102°. One recrystallization from chloroform gave an analytical sample, mp 101–102°; ir (Nujol) 1550 (vs, NH, amide II), 1640 (s, C=O, amide I), and 3430 (m, NH) cm^{-1}.

Anal. Calcd for $C_{28}H_{41}N_{14}O_{18}P \cdot 2H_2O$: C, 36.21; H, 4.88; Cl, none; N, 21.11; P, 3.33. Found: C, 35.58; H, 4.81; Cl, none; N, 21.12; P, 3.36.

The phosphonium salt **10d** is soluble in acetone, 2-propanol, and hot water, and insoluble in benzene and carbon tetrachloride.

Acid Hydrolysis of **3d**. A solution of **3d** (9.42 g, 0.02 mol) in 6*N* HCl (100 ml) was heated to reflux under argon in an oil bath, held at 110° for 20 h, and then stripped under vacuum. The residue, a green viscous mass (12.02 g), was digested three times with acetonitrile[29] (100 ml vols) and filtered hot, giving 3.08 g (0.045 mol, 22.0%) of methylamine hydrochloride, mp 230–231°, identified by ir.[30] The filtrate, concentrated to low volume and filtered again, yielded 2.14 g of a white, crystalline solid, mp 138–145°. The remainder (3.80 g) was a glassy, hygroscopic powder.[11]

Alkaline Hydrolysis of **5**, **6a–d** *and* **7a**. A solution of the 1,1-dimethylurea derivative **6c** (1.994 g, 5 mmol) in water (10 ml) deposited solids immediately upon treatment with a solution of sodium hydroxide (0.240 g, 6 mmol) in water (10 ml). The mixture was stirred for 30 min and filtered, giving 1.285 g (98.0%) of oxide-free triphenylphosphine, mp 79–80° (ir). The filtrate was neutralized with dilute HCl and stripped to dryness under vacuum, leaving a crystalline residue that was digested with hot chloroform, filtered to remove sodium chloride, and stripped again, giving 0.356 g (80.8%) of slightly impure 1,1-dimethylurea (**2c**), mp 180–181° after recrystallization from ethanol (lit.[31] mp 182°).

The 1,3-dimethylurea derivative **6d** afforded, under identical conditions, a mixture of 0.108 g (8.2%) of triphenylphosphine, mp 78–80°, and 1.186 g (85.2%) of triphenylphosphine oxide, mp 153–154°, separated by shaking with low-boiling petroleum ether, in which the oxide is insoluble.[32] The chloroform extract afforded 0.444 g (86.9%) of slightly impure 1,1,3-trimethylurea (**2f**), mp 71–73° after recrystallization from cyclohexane (lit.[33] mp 73.8°).

The same procedure was used with **5**, **6a** and **7a** (Table I).

Tris(ureidomethyl)phosphine Oxide (**13a**). A solution of **3a** (358.5 g, 1 mol) in water (120 ml) was treated under argon with 50% sodium hydroxide solution (80.0 g, 1 mol) over a 1 h period at room temperature, heated to 100° (no gassing), and allowed to cool. The product, mildly alkaline (pH 9.6) and giving a positive test for P(III) with iodine, was treated with 30% hydrogen peroxide (113.4 g, 1 mol) over a 1 h period at 20–30°. Ice-bath cooling was applied as needed to control the

exotherm. The resulting solution, still mildly alkaline (pH 8.6) but giving a negative test for P(III) with iodine, showed just two signals in the ^{31}P nmr: an intense signal for **13a** at 48.5 ppm, and a weak signal for unreacted **3a** at 29.5 ppm.

Tris(1,3-dimethylureidomethyl)phosphine Oxide (**13d**). The **3d** (11.77 g, 25 mmol) was added in portions to a solution of sodium hydroxide (1.00 g, 25 mmol) in water (25 ml). When the exotherm (to 46°) subsided, the solution was heated briefly to reflux in an oil bath, cooled, and stripped to dryness under vacuum. The residue (13.15 g) was taken up in methanol (75 ml), filtered to remove sodium chloride, and stripped again under vacuum. The residue, a solid white mass, was triturated under chloroform (100 ml), filtered, and rinsed thoroughly with chloroform, giving 8.63 g (98.5%) of **13d** as a white, crystalline solid, mp 226–227°d. A sample, recrystallized twice from ethanol (30 ml/g) and dried for 2 h at 100°, showed the same mp and ir spectrum. Ir (Nujol) 1170 (vs, P=O), 1545 (vs, NH, amide II), 1630 (s, C=O, amide I) and 3330 (m, NH) cm^{-1}; ^1H nmr (D_2O) δ 2.74 (s, 9H, 3-CH_3), 3.00 (s, 9H, 1-CH_3), and 3.93 (d, 6H, CH_2, $J = 2.5$ Hz); ^{31}P nmr (H_2O) δ 49.5.

Anal. Calcd for $C_{12}H_{27}N_6O_4P$: C, 41.13; H, 7.77; N, 23.99; P, 8.84; mol. wt., 350. Found: C, 41.06; H, 7.67; N, 23.83; P, 8.79; mol. wt. (osmometric in H_2O) 360, 355.

The phosphine oxide **13d** is soluble in water and methanol, and insoluble in all of the common organic solvents, including dimethylsulfoxide.

The chloroform filtrate and washings were combined and stripped, giving 2.44 g (95.7%) of 1,1,3-trimethylurea (**2f**), mp 66–69°.

1,1,3-Trimethylurea (**2f**). Features of the ^1H nmr spectrum of **2f** have been discussed in several papers,[34–37] but the data are insufficient for adequate characterization. The compound was prepared from methyl isocyanate and dimethylamine,[27] distilled under reduced pressure, and recrystallized from cyclohexane (15 ml/g), giving hygroscopic needles, mp 71–73° (lit.[33] mp 73.8°); ir[38] (Nujol) 1525 (vs, NH, amide II), 1610 (vs, C=O, amide I), and 3230 (s, NH) cm^{-1}; ^1H nmr ($CDCl_3$) δ 2.81 (d, 3H, 3-CH_3, $J = 4.0$ Hz, collapsing with D_2O to s, δ 2.81), 2.92 (s, 6H, 1-CH_3), and 5.08 (s, 1H, NH, vanishing with D_2O).

Tris(1,3,3-trimethylureidomethyl)phosphine Oxide (**13f**). Hydrolysis of **4f** (4.43 g, 0.01 mol) with sodium hydroxide (0.04 g, 0.01 mol) in water (25 ml), following the procedure given above for **13a**, gave 4.13 g of colorless oil which, upon shaking with acetone, deposited 1.03 g (26.2%) of **13f** as a white, crystalline solid, mp 190–191° after recrystallization from acetonitrile (12 ml/g); ir (Nujol) 1155 (vs, P=O) and 1650 (vs, C=O, amide I) cm^{-1}; ^1H nmr ($CDCl_3$) δ 2.85 (s, 18H, 3-CH_3), 3.08 (s, 9H, 1-CH_3), and 4.12 (d, 6H, CH_2, $J = 4.0$ Hz).

Anal. Calcd for $C_{15}H_{33}N_6O_4P$: C, 45.91; H, 8.48; N, 21.42; P, 7.89. Found: C, 46.06; H, 8.54, N, 21.36; P, 8.03.

The phosphine oxide **13f** is soluble in water, chloroform, and dioxane, and insoluble in acetone, ether, benzene and carbon tetrachloride. The oil from which **13f** was isolated, containing the corresponding tertiary phosphine **11f** (iodine test), yielded no tetramethylurea upon extraction with petroleum ether.

1-(Hydroxymethyl)-1,3-dimethylurea (**12d**). A solution of 1,3-dimethylurea (22.03 g, 0.25 mol), 37% formalin (20.29 g, 0.25 mol), and sodium hydroxide (0.5 g) in water (10 ml) was heated 2 h at 60°, cooled, neutralized to pH 7.0 with 6*N* HCl, and stripped in a rotary evaporator, giving 27.88 g (94.4%) of **12d**[39] as a colorless oil, $n^{20}D$ 1.4796; ir (neat) 1015 (s, br, OC), 1550 (vs, NH, amide II), 1640 (vs, C=O, amide I), and 3400 (vs, NH and OH) cm^{-1}; ^1H nmr ($CDCl_3$) δ 2.78 (d, 3H, 3-CH_3, $J = 4.0$ Hz, collapsing with D_2O to s, δ 2.80), 3.00 (s, 3H, 1-CH_3), 4.82 (s, 2H, CH_2), and 5.82 (m, 2H, NH and OH, vanishing with D_2O).

Anal. Calcd for $C_4H_{10}N_2O_2$: C, 40.66; H, 8.53; N, 23.72. Found: C, 40.57; H, 8.60; N, 24.18.

Methylenebis(1,3-dimethylurea) (**14d**). A solution of 1,3-dimethylurea (22.03 g, 0.25 mol), 37% formalin (10.14 g, 0.125 mol), and 6*N* HCl (5 ml) was heated 2 h at 60°, cooled, and stripped in a rotary evaporator, giving 24.42 g (103.8%) of a yellow oil that crystallized on standing. One recrystallization from acetonitrile (2 ml/g) gave 17.54 g (74.5%) of **14d** as a white, crystalline solid, mp 148–149°, unchanged by further recrystallization; ir (Nujol) 937 (s), 1020 (s, CN_2),[40] 1085 (s), 1140 (s, NCH_2N),[40] 1525 (vs, NH, amide II), 1630 (vs, C=O, amide I), and 3300 (s, NH) cm^{-1}; ^1H nmr[41] ($CDCl_3$) 2.79 (d, 6H, 3-CH_3, $J = 4.5$ Hz, collapsing with D_2O to s, δ 2.80), 3.01 (s, 6H, 1-CH_3), 4.81 (s, 2H, CH_2), and 6.32 (m, 2H, NH, vanishing with D_2O).

Anal. Calcd for $C_7H_{16}N_4O_2$: C, 44.66; H, 8.57; N, 29.77. Found: C, 44.96; H, 8.60; N, 29.67.

The diurea **14d** is soluble in water and chloroform, and insoluble in other common organic solvents. It dissolves in hot ethanol, 2-propanol, and acetic acid without separating on cooling, but can be recrystallized from acetonitrile, tetrachloroethylene, or $CHCl_3/CCl_4$.

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