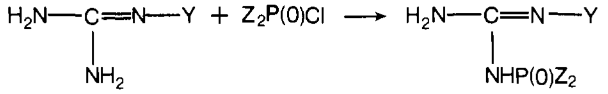
Preparation of Some Phosphinylguanidine Derivatives

Cletus E. Morris[1] **and Leon H. Chance**
Southern Regional Research Center,[2] New Orleans, La. 70179

2-Cyano-1-[bis(dimethylamino)phosphinyl]guanidine, 2-cyano-1-(diethoxyphosphinyl)guanidine, and 2-carbamoyl-1-(diethoxyphosphinyl)guanidine were prepared from cyanoguanidine or guanylurea. Successful phosphorylation of guanylurea required use of a dry, aprotic solvent. Ir spectral data are presented.

In the course of investigating compounds containing phosphorus and nitrogen as possible flame retardants for textiles, we prepared new compounds Ia–c from cyanoguanidine or guanylurea:



$$H_2N-\underset{\displaystyle NH_2}{\underset{|}{C}}=N-Y + Z_2P(O)Cl \longrightarrow H_2N-\underset{\displaystyle NHP(O)Z_2}{\underset{|}{C}}=N-Y$$

I

Ia Y = CN Z = NMe_2
Ib Y = CN Z = OEt
Ic Y = $C(O)NH_2$ Z = OEt

A search of the literature for compounds with structure I, where Y = CN or $C(O)NH_2$ and Z is alkoxy or aryloxy, revealed that only three such cyanoguanidine derivatives (Y = CN) and one such guanylurea derivative (Y = $C(O)NH_2$) have been reported (*1*), all of them containing aryloxy groups. Only three such aliphatic derivatives of guanidine (Y = H) have been reported (*2, 3*). No references to diaminophosphinyl derivatives of guanidine, cyanoguanidine, or guanylurea (I; Y = H, CN, or $C(O)NH_2$; Z = NH_2 or NR_2) could be found.

Beyer et al. (*1*) prepared 2-cyano-1-(diaryloxyphosphinyl)-guanidines by adding the diaryl phosphorochloridate to a solution of 1 mole of cyanoguanidine and 2 moles of sodium hydroxide in aqueous acetone. We used this procedure to prepare Ia and Ib, although the yields were rather poor. No such phosphorylations of guanylurea have been reported. [The 2-carbamoyl-1-(diaryloxyphosphinyl)guanidine reported by Beyer et al. (*1*) was prepared by hydrolysis of the corresponding cyanoguanidine.] (Dialkoxyphosphinyl)guanidines have been prepared by reacting dialkyl phosphorochloridates with guanidine in ethanol (*2, 3*). We tried to prepare Ic from diethyl phosphorochloridate and guanylurea in methanol or in a benzene–water mixture but were able to isolate only guanylurea salts. The desired product was obtained when a suspension of guanylurea in an aprotic solvent was used in the reaction. Yields were 13% using acetonitrile and 46% using dry acetone with precautions to exclude moisture from the system. The higher yield in the latter case was probably due to absence of moisture rather than to choice of solvent. In its sensitivity to moisture, this reaction resembles the phosphorylation of creatinine with diphenyl phosphorochloridate, which takes place only in a dry, aprotic solvent (*4*).

Ic was also prepared in low yield by hydrolyzing the corresponding cyanoguanidine (Ib).

Experimental

Melting points were determined in capillary tubes and are uncorrected. Elemental analyses were performed by Enviro Analytical Laboratory, Knoxville, Tenn. Elemental analyses (C, H, N, P) in agreement with theoretical values were obtained and submitted for review. Infrared spectra of samples in KBr disks were obtained with Perkin-Elmer Model 421 and 621 spectrometers. Qualitative solubilities were determined with 0.02 gram of solid in ca. 0.5 ml of solvent.

2-Cyano-1-[bis(dimethylamino)phosphinyl]guanidine (Ia). A solution of 17.1 grams (0.100 mole) of tetramethylphosphorodiamidic chloride (*5*) in 10 ml of dry acetone was added dropwise at 25–29°C in 32 min to a stirred solution of 8.4 grams (0.100 mole) of cyanoguanidine, 15.8 grams (0.200 mole) of 50.5% aqueous sodium hydroxide, 50 ml of acetone, and 40 ml of water. The mixture was stirred for 1 hr longer, then acidified with 6.0 grams (0.100 mole) of glacial acetic acid. Addition of a little more acetone induced crystallization. The mixture was cooled in ice water, filtered, and yielded 4.3 grams (20%) of crystals. Recrystallization from ethanol gave colorless crystals; mp 213°C (with gas evolution).

Ia is soluble in hot water, slightly soluble in hot ethanol, and practically insoluble in 2-propanol, acetone, acetonitrile, and chloroform. The ir spectrum showed absorption bands at 3340 (m), 3225 (m), 3160 (m), 2994 (w), 2948 (w), 2814 (w), 2344 (w), 2192 (s, C≡N), 1630 (s, NH_2), 1580 (vs), 1493 (s), 1400 (w), 1304 (s, CH_3), 1200 (s, P═O), 1170 (s, CH_3), 1064 (s, PNC), 996 (s), 946 (s), 860 (m), 762 (m), 691 (m), 670 (m), and 630 cm^{-1} (w).

2-Cyano-1-(diethoxyphosphinyl)guanidine (Ib). A solution of 17.29 grams (0.100 mole) of diethyl phosphorochloridate in 10 ml of acetone was added dropwise in 37 min to a stirred solution of 8.41 grams (0.100 mole) of cyanoguanidine, 15.69 grams (0.200 mole) of 51% aqueous sodium hydroxide, 42 ml of water, and 50 ml of acetone. During the addition the temperature rose to 47°C, and the two liquid phases initially present coalesced. The solution was stirred for 30 min longer and poured into 300 ml of water. Acidification with 17.73 grams (0.106 mole) of 36% acetic acid did not lead to separation of a product. The solution was evaporated in a stream of air until crystallization was observed, then chilled, and filtered to obtain 6.54 grams (29.7%) of crystals; mp 164–165.5°C. The product was recrystallized from acetone: mp 164–165°C.

Ib is soluble in ethanol, 2-ethoxyethanol, hot water, hot 2-propanol, hot acetone, and hot acetonitrile, and practically insoluble in chloroform. The ir spectrum showed absorption bands at 3401 (m), 3329 (w), 3190 (m), 3170 (m), 3071 (w), 2993 (w), 2968 (w), 2885 (w), 2776 (w), 2214 (s, C≡N), 2182 (sh), 1662 (s, NH_2), 1599 (s), 1516 (vs), 1446 (w), 1393 (m), 1243 (s, P═O), 1160 (w, POEt), 1044 (vs, POC), 977 (s), 859 (w), 801 (w), 756 (m), 696 (w), 660 (w), and 580 cm^{-1} (m).

Unsuccessful reaction of diethyl phosphorochlororidate with guanylurea in methanol. A solution of 1.08 grams (0.0200 mole) of sodium methoxide in 10 ml of methanol was

---

[1] To whom correspondence should be addressed.

[2] One of the facilities of the Southern Region, Agricultural Research Service, U.S. Department of Agriculture.

added to a suspension of 3.02 grams (0.0100 mole) of guanylurea sulfate in 35 ml of methanol. The mixture was stirred for 2 hr, heated to boiling, allowed to cool to 45°C, and filtered to remove sodium sulfate.

Triethylamine (2.09 grams, 0.0207 mole) was added to the guanylurea solution; then 3.47 grams (0.0201 mole) of diethyl phosphorochloridate in 5 ml of acetone was added dropwise in 5 min as the temperature rose to 41°C. The mixture was stirred 30 min and allowed to stand overnight. Solvent was removed by a rotary evaporator, and the residue was washed twice with chloroform to remove triethylamine hydrochloride. This left 1.94 grams (70%) of guanylurea hydrochloride, which was recrystallized from ethanol and identified by elemental analyses, ir, and qualitative tests for guanylurea (Ni complex formation) and chloride ion.

***2-Carbamoyl-1-(diethoxyphosphinyl)guanidine* (*Ic*).** *From guanylurea.* A solution of guanylurea in methanol was prepared essentially as described above, and solvent was removed by a rotary evaporator. Recrystallization of the residue from ethanol gave guanylurea in 75% yield.

Under a nitrogen atmosphere 5.64 grams (0.0552 mole) of guanylurea, 85 ml of dry acetone, and 5.97 grams (0.0590 mole) of triethylamine were placed in a 200-ml flask equipped with a mechanical stirrer, a thermometer, a dropping funnel, a nitrogen inlet, and a drying tube. A solution of 9.53 grams (0.0552 mole) of diethyl phosphorochloridate in 10 ml of acetone was added dropwise to the stirred suspension in 13 min. The flask was cooled intermittently in an ice bath to hold the temperature at 27–30°C. The suspension was stirred for 2 hr longer, allowed to stand overnight, and filtered. The residue was washed with acetone and recrystallized from chloroform to obtain 2.61 grams of crystals; mp 164–165°C (cloudy melt). More Ic was isolated from the mother liquor and the acetone solution; the total yield of material with mp above 164° was 6.08 grams (46.2%). The mp of Ic prepared from guanylurea was not depressed on mixture with Ic prepared by hydrolysis of Ib.

From Ib. A mixture of 4.40 grams (0.0200 mole) of Ib, 1.91 grams of 38% hydrochloric acid, and 60 ml of ethanol was stirred and heated under reflux for 30 min, and then evaporated overnight in a stream of air. The residual paste was stirred with acetone and filtered. The unidentified acetone-insoluble material, mp 257–260°C, weighed 0.18 gram. The acetone solution was evaporated, water was added, and the resulting crystals were collected and recrystallized from methanol to obtain 0.30 gram (7%) of Ib, mp 161–163°C. Crystals obtained from the water and methanol mother liquors were combined and recrystallized from water and from acetone to obtain 0.28 gram (6%) of Ic; mp 164.5–165°C (cloudy melt, solidifying at higher temperatures and remelting near 245°C). The analytical sample was recrystallized from acetone: mp 170–170.5°C (cloudy melt).

Increasing the reaction time to 3 hr did not increase the amount of Ic isolated, but in this case, no Ib was recovered. The unidentified acetone-insoluble product was again isolated in low yield.

Ic is soluble in 2-ethoxyethanol, warm ethanol, hot water, and hot 2-propanol, slightly soluble in hot acetone and hot acetonitrile, and practically insoluble in chloroform. The ir spectrum showed absorption bands at 3406 (s, NH), 3315 (m, NH), 3262 (m), 2989 (w), 1717 (s), 1646 (vs), 1619 (m), 1570 (s), 1446 (m), 1389 (w), 1318 (m), 1202 (s, P=O), 1165 (w, POEt), 1024 (s, POC), 968 (m), 948 (m), 870 (m), 796 (w), 762 (w), 686 (w), 585 (w), 527 (w), and 500 cm^{-1} (m).

Acknowledgment

The authors thank Elizabeth R. McCall and Nancy M. Morris for the ir spectra.

Literature Cited

(1) Beyer, H., Pyl, T., Lemke, H., *J. Prakt. Chem.*, **16**, 132 (1962).
(2) Cates, L. A., Ferguson, N. M., *J. Pharm Sci.*, **55**, 966 (1966).
(3) Cramer, F., Vollmar, A., *Chem. Ber.*, **91**, 911 (1958).
(4) Sasse, K., in "Methoden der Organischen Chemie (Houben-Weyl)," Vol 12, Part 2, p 520, E. Muller, Ed., Georg Thieme Verlag, Stuttgart, Germany, 1964.
(5) Walsh, E. N., Toy, A.D.F., *Inorg. Syn.*, **7**, 71 (1963).

Received for review January 13, 1975. Accepted June 7, 1975.