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A Challenging Synthetic Approach to Phosphonium Ylide-Betaines of the Pyrimidine Series

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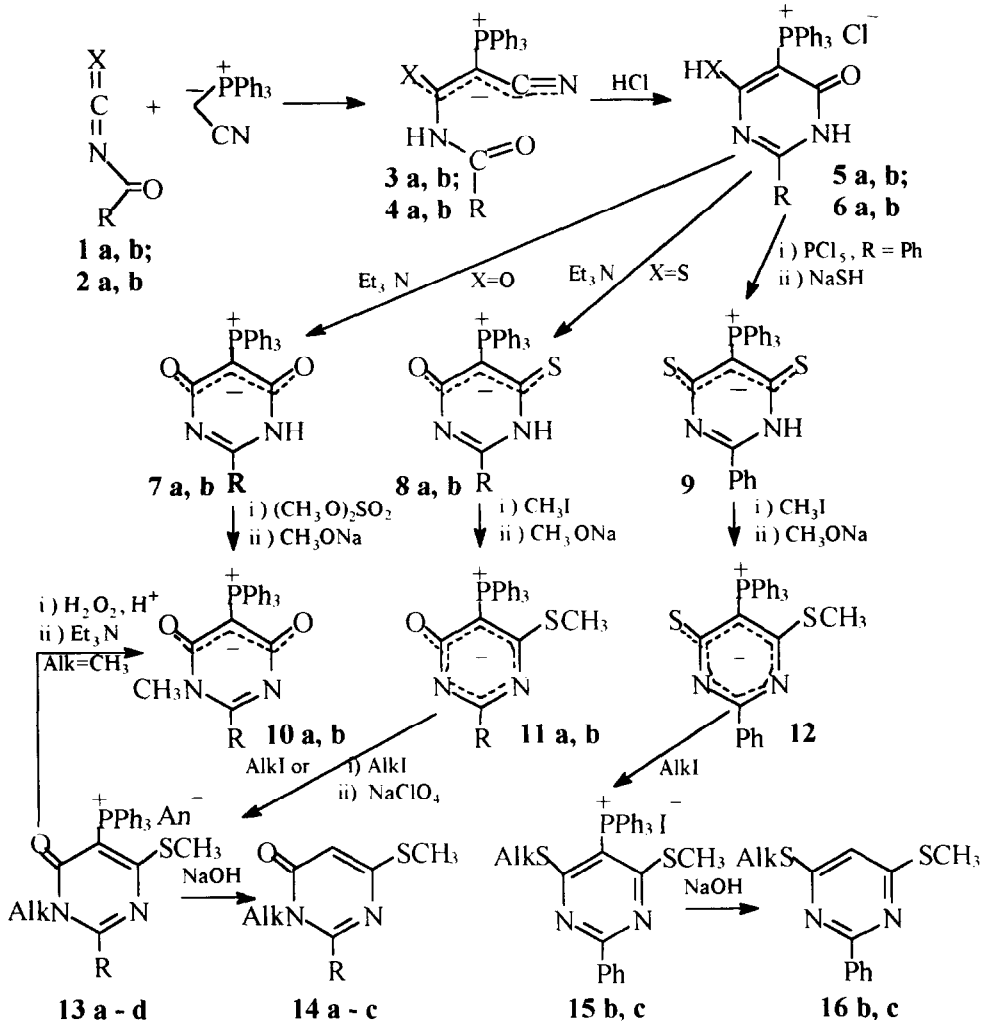
Abstract: Adducts of the available ylide $Ph_3\overset{+}{P}\text{-}\overset{-}{C}HCN$ with acylisocyanates and their thio analogues undergo facile cyclization, promoted by hydrogen chloride in methanol, to give high yields of 2-alkyl(aryl)-4-hydroxy(mercapto)-6-oxo-1,6-dihydropyrimidin-5-yl-triphenyl-phosphonium chlorides suitable to prepare several types of phosphonium ylide-betaines of the pyrimidine series, the structure of which was established by chemical transformations and X-ray diffraction analysis. Despite the mesomeric character of these heterocyclic nucleophilic agents, they are alkylated in a regioselective manner, which proves this approach to be important for the synthesis of non-phosphorylated pyrimidine derivatives, which are otherwise difficult to obtain.

A systematic investigation of the chemical transformations of phosphonium ylide-betaines with general formula $Ph_3\overset{+}{P}\text{-}\overset{-}{Het}$ has shown that often they are irreplaceble reagents for the synthesis of many functionally substituted 1,3-azoles (see review[1] and reports[2-9]). Until recently, such transformations have played no appreciable role in the preparative chemistry of azines, as there were no convenient methods for the preparation of the appropriate ylide-betaines. In the present work, we report a promising synthetic approach to various phosphonium ylide-betaines of the pyrimidine series, based on readily available addition products of the well known ylide, $Ph_3\overset{+}{P}\text{-}\overset{-}{C}HCN$, and acyl isocyanates **1** or acyl isothiocyanates **2** (see Scheme). Analogues of adducts **3** and **4** were already reported in the literature[10-13] and some of them were converted to various heterocyclic compounds[14-18]. Nevertheless, the transformations **3** → **5** and **4** → **6** promoted by hydrogen chloride in methanol (see Scheme) are observed for the first time. The involvement of the cyano and amide groups in the ring formation was confirmed by IR spectroscopy. However, in order to establish reliably the structure of the cyclization products, we subjected them to dehydrochlorination and performed an X-ray diffraction analysis of the resulting compounds **7a** and **8a**, thereby identifying them unambiguously as pyrimidine derivatives (see Tables 1, 2 and Figs 1, 2).

From the lengths of the most important bonds C(5)-P, C(4)-O, and C(6)-O in **7a** of 1.746(3), 1.253(3), and 1.240(3)Å, respectively, we conclude that **7a** is best represented as a stabilized ylide, and that the betaine resonance structures, though essential, only play a minor role (for generalized X-ray data of

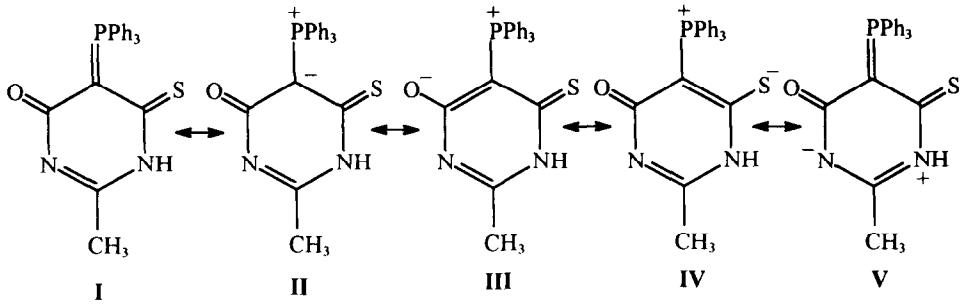


X = O (**1, 3, 5**) , S (**2, 4, 6**) ;

a: R = CH_3 (**3 - 8, 10, 11, 13, 14**); Alk = R = CH_3 , An = I (**13**); Alk = R = CH_3 (**14**);
b: R = C_6H_5 (**3 - 8, 10, 11, 13, 14**); Alk = CH_3, R = C_6H_5, An = I (**13**); Alk = CH_3, R = C_6H_5 (**14**), Alk = CH_3 (**15, 16**);
c: Alk = C_2H_5, R = C_6H_5, An = I (**13**); Alk = C_2H_5, R = C_6H_5 (**14**), Alk = C_2H_5 (**15, 16**);
d: Alk = R = CH_3, An = ClO_4 (**13**).

Scheme

ylides see monograph[19]). Interestingly, the role of the betaine structures increases for compound **8a**, which crystallizes to give four molecules (A-D) in the asymmetric unit, mainly differing by the conformation of the phenyl rings in the triphenylphosphonium group. In two of them (conformations B, C) the ylide bond length is 1.777(4)Å, close to the extreme value of 1.78(1)Å found in a superstabilized selenium-containing phosphonium ylide[20] and to the single bond C(5)-P, 1.793(5)Å, in phosphonium salt **13d** obtained by the sequence **8a** → **11a** → **13a** → **13d** outlined in the Scheme. To rationalize the data obtained for **8a**, we can consider five resonance structures I-V:



Since the C(5)-P bond in **8a** proved to be much closer to a single rather than to a double linkage, structures I and V are of little importance. The contribution of the ylide structure II is also not significant, as compound **8a** and its closest analogues do not enter into a Wittig reaction with *p*-nitrobenzaldehyde even on prolonged heating. Of the remaining two structures III and IV, preference should be given to the latter because the C-S bond length (1.67-1.69 Å) is closer to a single rather than to a double bond. This is in full agreement with the observation that a thiocarbonyl substituent stabilizes the ylide center more efficiently than does a carbonyl group, as was shown previously for mesomeric phosphonium ylides of the azole series[9].

Differences in the electron density distribution in mesomeric ylide-betaines **7** and **8**, as well as in the "hardness" of their nucleophilic centers, have an effect on the attitude of these compounds towards electrophilic agents. Thus, they are methylated quite regioselectively, but at different centers (cf. transformations **7** → **10** and **8** → **11** in the Scheme). The structure of the methylation product derived from **8a** and after abstraction of hydrogen iodide, was established by X-ray diffraction showing methylation in ylide-betaine **11a** at the sulfur atom (see Table 3 and Fig. 3). Further alkylation of the mesomeric compound **11a** and its analogues proceeds also in a regioselective manner at the ring nitrogen atom next to the carbonyl group (see Table 4 and Fig. 4 for X-ray analysis of **13d**).

Table 1. Selected Bond Lengths (Å) and Angles (°) for Ylide-Betaine **7a**

N(1)-C(2)	1.295(3)	C(5)-C(6)	1.444(4)
N(1)-C(6)	1.398(3)	C(6)-O(9)	1.240(3)
C(2)-N(3)	1.358(3)	C(5)-P(10)	1.746(3)
C(2)-C(7)	1.490(4)	P(10)-C(11)	1.798(3)
N(3)-C(4)	1.376(3)	P(10)-C(17)	1.814(3)
C(4)-O(8)	1.253(3)	P(10)-C(23)	1.805(3)
C(4)-C(5)	1.410(4)		
N(1)-C(2)-N(3)	124.0(2)	O(9)-C(6)-C(5)	122.1(2)
N(1)-C(2)-C(7)	120.5(2)	O(9)-C(6)-N(1)	119.3(2)
C(2)-N(3)-C(4)	122.9(2)	C(4)-C(5)-P(10)	120.2(2)
N(3)-C(4)-C(5)	114.9(2)	C(6)-C(5)-P(10)	119.7(2)
O(8)-C(4)-C(5)	126.1(2)	C(5)-P(10)-C(11)	112.1(1)
C(4)-C(5)-C(6)	119.9(2)	C(5)-P(10)-C(17)	110.4(1)
N(1)-C(6)-C(5)	118.6(2)	C(5)-P(10)-C(23)	109.8(1)

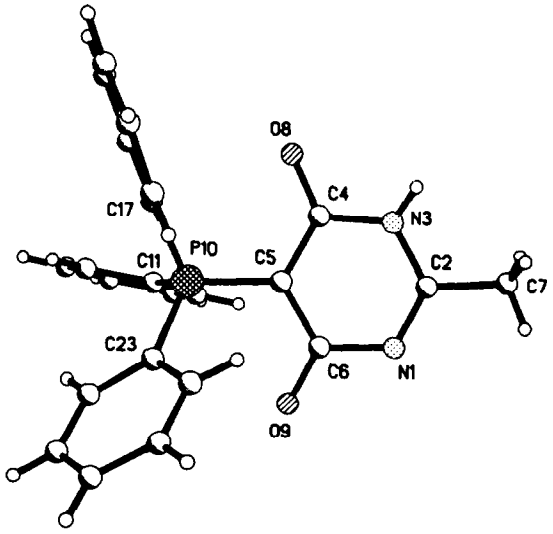


Fig. 1. Molecular Structure of Ylide-Betaine **7a**

Table 2. Selected Bond Lengths (Å) and Angles (°) for Ylide-Betaine **8a** (Conformations A, B, C and D)

	A	B	C	D
N(1)-C(2)	1.297(5)	1.298(5)	1.297(5)	1.296(5)
N(1)-C(6)	1.398(5)	1.385(5)	1.394(5)	1.397(5)
C(2)-N(3)	1.342(5)	1.351(5)	1.355(5)	1.349(5)
C(2)-C(7)	1.490(5)	1.487(6)	1.484(6)	1.492(5)
N(3)-C(4)	1.374(5)	1.377(5)	1.374(5)	1.383(5)
C(4)-S(8)	1.684(4)	1.675(4)	1.686(4)	1.673(4)
C(4)-C(5)	1.402(5)	1.415(6)	1.401(5)	1.405(5)
C(5)-C(6)	1.444(5)	1.436(6)	1.440(5)	1.447(5)
C(6)-O(9)	1.230(4)	1.247(5)	1.244(4)	1.238(4)
C(5)-P(10)	1.754(4)	1.777(4)	1.777(4)	1.755(4)
P(10)-C(11)	1.810(4)	1.807(4)	1.805(4)	1.808(4)
P(10)-C(17)	1.799(4)	1.802(4)	1.810(4)	1.806(4)
P(10)-C(23)	1.808(4)	1.818(5)	1.802(4)	1.804(7)
N(1)-C(2)-N(3)	123.2(3)	123.3(4)	123.2(4)	123.2(3)
N(1)-C(2)-C(7)	119.9(3)	119.8(4)	120.1(4)	119.9(4)
C(2)-N(3)-C(4)	123.1(3)	123.8(3)	123.5(3)	123.1(3)
N(3)-C(4)-C(5)	114.4(3)	114.5(3)	115.1(3)	114.0(3)
N(3)-C(4)-S(8)	119.4(3)	118.8(3)	118.9(3)	119.9(3)
C(4)-C(5)-C(6)	119.0(3)	119.9(4)	120.0(4)	118.9(3)
N(1)-C(6)-C(5)	116.7(3)	119.7(3)	119.0(3)	116.9(3)
O(9)-C(6)-C(5)	123.6(3)	122.7(4)	123.8(4)	123.7(3)
O(9)-C(6)-N(1)	119.6(3)	117.5(3)	117.2(3)	119.4(3)
C(4)-C(5)-P(10)	121.8(3)	119.1(3)	117.8(3)	120.8(3)
C(6)-C(5)-P(10)	119.0(3)	120.9(3)	121.8(3)	119.9(3)
C(5)-P(10)-C(11)	107.8(2)	112.0(2)	111.6(2)	111.1(2)
C(5)-P(10)-C(17)	112.7(2)	110.4(2)	109.7(2)	113.0(2)
C(5)-P(10)-C(23)	110.4(2)	112.0(2)	112.5(2)	109.0(2)

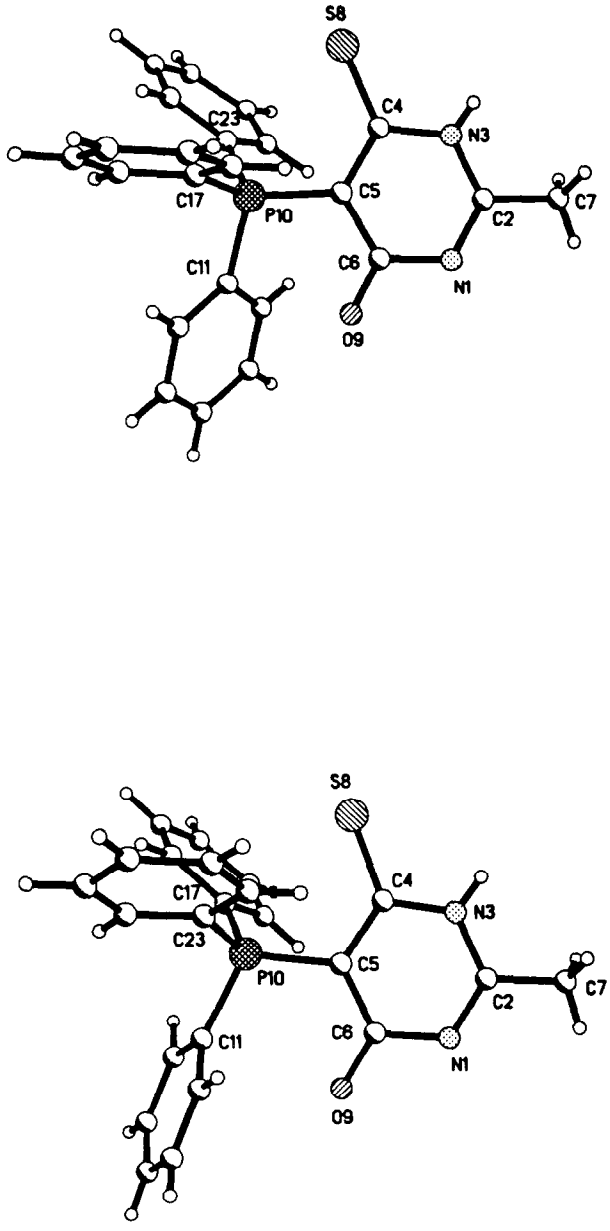


Fig. 2. Molecular Structure of Ylide-Betaine **8a** (Conformations A (top) and C (bottom))

Table 3. Selected Bond Lengths (Å) and Angles (°) for Ylide-Betaine **11a**

N(1)-C(2)	1.312(5)	C(5)-C(6)	1.440(5)
C(2)-N(3)	1.344(5)	C(6)-O(29)	1.244(4)
C(2)-C(7)	1.495(6)	N(1)-C(6)	1.375(5)
N(3)-C(4)	1.331(5)	C(5)-P(10)	1.775(4)
C(4)-S(8)	1.765(4)	P(10)-C(11)	1.805(4)
C(4)-C(5)	1.405(5)	P(10)-C(17)	1.804(4)
P(10)-C(23)	1.802(4)		
N(1)-C(2)-N(3)	127.4(3)	O(29)-C(6)-C(5)	120.6(3)
N(1)-C(2)-C(7)	116.7(4)	O(29)-C(6)-N(1)	120.9(3)
C(2)-N(3)-C(4)	116.8(3)	C(4)-C(5)-P(10)	131.6(3)
N(3)-C(4)-S(8)	116.4(3)	C(6)-C(5)-P(10)	111.0(3)
N(3)-C(4)-C(5)	121.7(3)	C(5)-P(10)-C(11)	111.4(2)
C(4)-C(5)-C(6)	117.3(3)	C(5)-P(10)-C(17)	108.8(2)
N(1)-C(6)-C(5)	118.5(3)	C(5)-P(10)-C(23)	113.7(2)

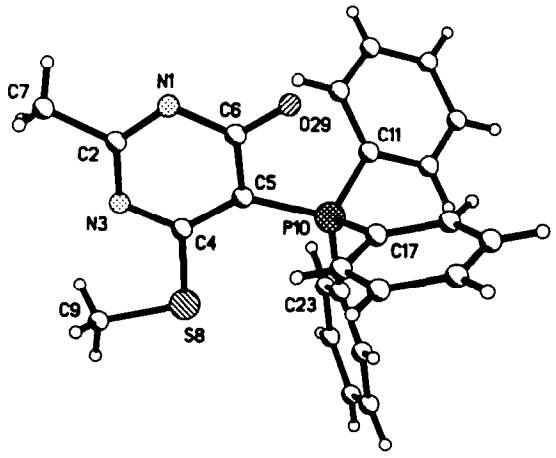


Fig. 3. Molecular Structure of Ylide-Betaine **11a** (acetonitrile and water molecules not shown)

Table 4. Selected Bond Lengths (Å) and Angles (°) for Phosphonium Salt **13d**

N(1)-C(2)	1.330(7)	C(4)-C(5)	1.365(7)
N(1)-C(6)	1.418(7)	C(5)-C(6)	1.468(7)
N(1)-C(7)	1.488(7)	C(6)-O(30)	1.205(6)
C(2)-N(3)	1.302(7)	C(5)-P(11)	1.793(5)
C(2)-C(8)	1.504(8)	P(11)-C(12)	1.804(5)
N(3)-C(4)	1.363(7)	P(11)-C(18)	1.795(5)
C(4)-S(9)	1.745(5)	P(11)-C(24)	1.795(6)
S(9)-C(10)	1.792(6)		
N(1)-C(2)-N(3)	124.1(5)	O(30)-C(6)-C(5)	125.8(5)
N(1)-C(2)-C(8)	118.4(5)	O(30)-C(6)-N(1)	121.1(5)
C(2)-N(3)-C(4)	118.8(5)	C(4)-C(5)-P(11)	130.0(4)
N(3)-C(4)-S(9)	113.7(4)	C(6)-C(5)-P(11)	110.3(4)
N(3)-C(4)-C(5)	121.8(5)	C(5)-P(11)-C(12)	107.5(2)
C(4)-C(5)-C(6)	119.7(5)	C(5)-P(11)-C(18)	110.5(2)
N(1)-C(6)-C(5)	113.1(5)	C(5)-P(11)-C(24)	111.9(2)

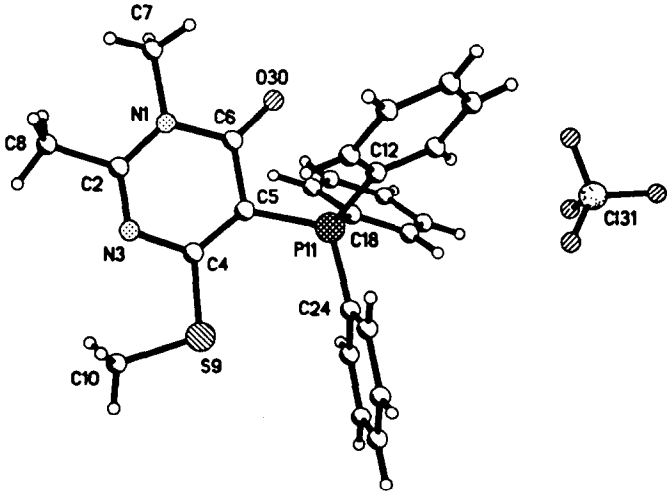


Fig. 4. Molecular Structure of Phosphonium Salt **13d**

The structure determination of **13d** was also useful for the identification of compounds **10** obtained by two independent ways, **7** → **10** ← **13**, leaving no doubt to the N-methylation of the mesomeric ylide-betaines **7a,b**.

Thus, the ylide-betaines **7-12** have been successfully applied in the regioselective synthesis of many new phosphorus-containing pyrimidine derivatives. Their separation and purification are considerably facilitated by the occurrence of the onium group in the molecules. The products containing no labile hydrogen atoms are readily dephosphorylated in alkaline medium, which can be used for the preparation of the otherwise not easily accessible sulfur-containing pyrimidine bases **14** and **16**.

It is worth pointing out that the transformation sequences **8** → **11** → **13** → **14** and **9** → **12** → **15** → **16** presented in the Scheme were found to be useful models in phosphonium syntheses of nucleoside analogues, which will be reported in the near future.

EXPERIMENTAL SECTION

X-ray Structural Analysis of **7a**, **8a**, **11a**, *and* **13d**:[21]

Cell constants and reflections were measured with a Siemens P4-PC four-circle diffractometer (graphite monochromator, λ(Cu-Kα) = 1.541781Å). Lattice parameters were obtained from least-squares of 25 reflections (for **7a**, $12 < 2\theta < 30°$) and 20 reflections (for **8a**, $9 < 2\theta < 30°$; for **11a**, $21 < 2\theta < 37°$; for **13d**, $15 < 2\theta < 30°$). The structures were solved by direct methods and refined by full-matrix least-squares on F^2 using SHELXL-93.[22] Hydrogen atoms were refined in the riding mode allowing the X-H distances to refine (except for **13d**). Non-hydrogen atoms were refined anisotropic; hydrogen atoms with U 1.2 times U_{eq} of the parent atom, except for **7a** where U was refined independently. The program package SHELXTL-PC was used for other calculations and drawings.[23]

(**7a**): $C_{23}H_{19}N_2O_2P$, MW=386.39, a white crystal of 0.20 x 0.20 x 0.50 mm size, space group $P2_1/c$, Z=4, monoclinic, a = 12.016(1), b = 8.317(1), c = 19.623(1) Å, β = 99.74(1)°, V = 1932.8(3) Å^3, d_{calc} = 1.328 g cm^{-3}, F(000) = 808, T = 289K, ω-scan, Δω = 0.60°, $2.0 < \omega < 60.0°$ min^{-1}, $7.4 < 2\theta < 100.9°$, 2925 collected reflections ($(\sin\theta/\lambda)_{max}$ = 0.50), 2029 independent reflections (R_{int} = 4.5%). Final R-values: R_1=0.0454, wR_2=0.1194 for all reflections.

(8a): $C_{23}H_{19}N_2OPS \cdot 1/2H_2O$, MW=411.46, a light yellow crystal of 0.30 x 0.40 x 0.40 mm size, space group P-1, Z=8, triclinic, a = 16.917(1), b = 17.035(1), c = 17.370(1) Å, α = 102.80(1), β = 115.75(1), γ = 100.79(1)°, V = 4161.3(4) Å^3, d_{calc} = 1.313 g cm^{-3}, F(000) = 1720, T = 289K, ω-scan, $\Delta\omega$ = 0.60°, 2.0 < ω < 60.0° min^{-1}, 5.6 < 2θ < 100.9°, 9665 collected reflections ($(\sin\theta/\lambda)_{max}$ = 0.50), 8544 independent reflections (R_{int} = 4.0%). Final R-values: R_1=0.0558, wR_2=0.1448 for all reflections.

(11a): $C_{24}H_{21}N_2OPS \cdot CH_3CN \cdot H_2O$, MW=475.55, a light yellow crystal of 0.30 x 0.30 x 0.40 mm size, space group $P2_1/c$, Z=4, monoclinic, a = 15.574(1), b = 8.957(1), c = 17.636(2) Å, β = 97.30(1)°, V = 2440.2(4) Å^3, d_{calc} = 1.294 g cm^{-3}, F(000) = 1000, T = 289K, ω-scan, $\Delta\omega$ = 0.60°, 2.5 < ω < 60.0° min^{-1}, 5.8 < 2θ < 100.9°, 3621 collected reflections ($(\sin\theta/\lambda)_{max}$ = 0.50), 2520 independent reflections (R_{int} = 5.3%). Final R-values: R_1=0.0559, wR_2=0.1547 for all reflections.

(13d): $C_{25}H_{24}ClN_2O_5PS$, MW=514.97, a light yellow crystal of 0.15 x 0.15 x 0.30 mm size, space group $P2_1/n$, Z=4, monoclinic, a = 10.304(1), b = 10.663(1), c = 23.080(1) Å, β = 92.50(2)°, V = 2533(1) Å^3, d_{calc} = 1.392 g cm^{-3}, F(000) = 1104, T = 289K, ω-scan, $\Delta\omega$ = 0.75°, 2.0 < ω < 60.0° min^{-1}, 7.6 < 2θ < 100.9°, 3670 collected reflections ($(\sin\theta/\lambda)_{max}$ = 0.50), 2660 independent reflections (R_{int} = 12.0%). Final R-values: R_1=0.0842, wR_2=0.1637 for all reflections.

IR spectra: Specord M-80; KBr tablets. *UV spectra*: Specord UV-VIS. *^{1}H NMR spectra*: Varian Gemini (200 MHz); δ-scale; internal reference hexamethyldisiloxane.

2-Acylamino-1-cyano-2-oxo(thioxo)ethylidenetriphenylphosphoranes* (3a,b; 4a,b):

General procedure. To a suspension of cyanomethylenetriphenylphosphorane (0.01 mol) in acetonitrile (150 ml) is added a solution of the appropriate acyl isocyanate or acyl isothiocyanate (0.01 mol) in acetonitrile (70 ml). The mixture is kept at 50 to 70°C for 3 h, the solvent evaporated in vacuum, and the residue purified by crystallization.

2-Acetylamino-1-cyano-2-oxoethylidenetriphenylphosphorane (3a):

Yield 92%, mp 212-214°C (from acetonitrile). IR: 2180 (C≡N), 1730 (NC=O), 1640 ($^-$CC=O) cm^{-1}. (Found: C, 71.97; H, 5.08; N, 7.39; P, 8.02. Calc for $C_{23}H_{19}N_2O_2P$ (MW 386.39): C, 71.50; H, 4.96; N, 7.25; P, 8.02%).

* Hereafter, the name of only one nonpolar resonance structure is given for mesomeric compounds.

2-Benzoylamino-1-cyano-2-oxoethylidenetriphenylphosphorane (3b):
Yield 95%, mp 214-216°C (from acetonitrile). IR: 2185 (C≡N), 1675 (NC=O), 1585 (CC=O) cm^{-1}. (Found: N, 6.25; P, 6.80. Calc for $C_{28}H_{21}N_2O_2P$ (MW 448.60): N, 6.25; P, 6.91%).

2-Acetylamino-1-cyano-2-thioxoethylidenetriphenylphosphorane (4a):
Yield 72%, mp 201-203°C (from ethanol). IR: 2195 (C≡N), 1690 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): 2.35 (s, CH_3), 7.52-7.84 (m, $3C_6H_5$), 8.61 (s, NH). (Found: N, 6.88; P, 7.87; S, 7.92. Calc for $C_{23}H_{19}N_2OPS$ (MW 402.45): N, 6.96; P, 7.70; S, 7.97%).

2-Benzoylamino-1-cyano-2-thioxoethylidenetriphenylphosphorane (4b):
Yield 70%, mp 167-169°C (from ethanol). (Found: N, 5.92; P, 6.76; S, 6.81. Calc for $C_{28}H_{21}N_2OPS$ (MW 464.50): N, 6.03; P, 6.67; S, 6.90%).

2-R-4,6-Dioxo-5-triphenylphosphoranylidene-1,4,5,6-tetrahydropyrimidines (7a,b): General procedure. A suspension of **3a** or **3b** (0.01 mol) in absolute methanol (25 ml) is saturated with dry hydrogen chloride for 4 h. Methanol and excess hydrogen chloride are removed in vacuum and to the residue preliminarily dissolved in methanol (50 ml) is added a solution of triethylamine (0.02 mol) in methanol (10 ml). The mixture is allowed to stand at 20 to 25°C for 4 h. The solvent and excess triethylamine are evaporated in vacuum and the residue is washed with water and crystallized.

2-Methyl-4,6-dioxo-5-triphenylphosphoranylidene-1,4,5,6-tetrahydropyrimidine (7a): Yield 82%, mp 142-144°C (from ethanol). IR: no intense absorption in the region of 1620-2400 cm^{-1}. ^1H NMR ($CDCl_3$): 2.07 (s, CH_3), 7.5-7.7 (m, $3C_6H_5$). (Found: C, 71.95; H, 5.16; N, 7.24; P, 8.16. Calc for $C_{23}H_{19}N_2O_2P$ (MW 386.39): C, 71.50; H, 4.96; N, 7.25; P, 8.02%).

4,6-Dioxo-2-phenyl-5-triphenylphosphoranylidene-1,4,5,6-tetrahydropyrimidine (7b):
Yield 94%, mp 314-316°C (from acetonitrile). IR: no intense absorption in the region of 1620-2300 cm^{-1}. (Found: N, 6.20; P, 6.66. Calc for $C_{28}H_{21}N_2O_2P$ (MW 448.60): N, 6.25; P, 6.91%).

2-R-4-Oxo-6-thioxo-5-triphenylphosphoranylidene-1,4,5,6-tetrahydropyrimidines (8a,b):
General procedure. To a suspension of **4a** or **4b** (0.01 mol) in methanol (150 ml) is added 36% hydrochloric acid (2 ml) and, after stirring the mixture at 20 to 25°C for 5 h, methanol and excess hydrochloric acid are evaporated in vacuum. The residue is dissolved in methanol (50 ml), and triethylamine (0.015 mol) is added. The mixure is allowed to stand at 20 to 25°C for 4 h, then the solvent is removed in

vacuum, the residue washed with water, crystallized from acetonitrile or ethanol, and dried at 100 to 120°C (0.1 mm Hg) for 4 to 5 h.

2-Methyl-4-oxo-6-thioxo-5-triphenylphosphoranylidene-1,4,5,6-tetrahydropyrimidine (8a):

Yield 95%, mp 273-276°C (from acetonitrile). IR: 1652 (C=O), 3450 (N-H) cm^{-1}. ^1H NMR ($CDCl_3$): 2.16 (s, CH_3), 7.53-7.67 (m, $3C_6H_5$), 11.95 (s, NH). (Found: C, 68.70; H, 4.81; P, 7.80; S, 7.81. Calc for $C_{23}H_{19}N_2OPS$ (MW 402.46): C, 68.64; H, 4.76; P, 7.70; S, 7.97%). A sample of compound **8a** prepared by the general procedure and thoroughly dried was found to be unsuitable for X-ray diffraction analysis. An appropriate sample in the form of solvate **8a**·$1/2H_2O$ was obtained by dissolving wet **8a** (1 g) in acetonitrile (15 ml) on heating, keeping the solution for 12 h heated, careful filtering of the crystals formed, followed by drying at 20°C (1 mm Hg) for 1 h. (Found: C, 67.09; H, 4.83. Calc for $C_{23}H_{19}N_2OPS·1/2H_2O$ (MW 411.46): C, 67.14; H, 4.90%).

4-Oxo-2-phenyl-6-thioxo-5-triphenylphosphoranylidene-1,4,5,6-tetrahydropyrimidine (8b):

Yield 88%, mp 268-270°C (from ethanol). (Found: N, 5.87; P, 6.79; S, 6.96. Calc for $C_{28}H_{21}N_2OPS$ (MW 464.53): N, 6.03; P, 6.67; S, 6.90%).

2-Phenyl-4,6-dithioxo-5-triphenylphosphoranylidene-1,4,5,6-tetrahydropyrimidine (9):

A suspension of **3b** (0.01 mol) in absolute methanol (25 ml) is saturated with dry hydrogen chloride for 4 h after which the solvent and excess hydrogen chloride are removed in vacuum. To the residue dissolved in phosphorus oxychloride (25 ml) is added phosphorus pentachloride (0.022 mol). The mixture is refluxed for 5 h, phosphorus oxychloride evaporated in vacuum, the residue washed several times with diethyl ether, dried in vacuum, and dissolved in anhydrous dimethylformamide (50 ml). Sodium hydrosulfide (0.033 mol) is added to the resulting stirred solution and the mixture is further stirred at 20 to 25°C for 6 h, poured into water (500 ml), the precipitate filtered off and crystallized twice from acetonitrile. Yield 88%, mp 275-277°C. IR: no intense absorption in the region of 1620-2300 cm^{-1}. (Found: N, 5.92; P, 6.26; S, 13.26. Calc for $C_{28}H_{21}N_2PS_2$ (MW 480.60): N, 5.83; P, 6.44; S, 13.34%).

2-R-3-Methyl-4,6-dioxo-5-triphenylphosphoranylidene-1,4,5,6-tetrahydropyrimidines (10a,b):

General procedure. Method A. A mixture of **7a** or **7b** (0.01 mol) and freshly distilled dimethyl sulfate (5 ml) is allowed to stand at 20 to 25°C for 15 h after which it is poured into anhydrous diethyl ether (150 ml). The precipitate is filtered off, dried in vacuum over phosphorus pentoxide and dissolved in dry acetonitrile (50 ml). The solution is cooled to 0°C and mixed with sodium methoxide (0.011 mol) in methanol (0.5 ml). The mixture is kept at 0°C for 2 h, the solvent evaporated in vacuum and the product purified by crystallization.

Method B. To an ice-cold suspension of **13a** or **13b** (see below) (0.01 mol) in glacial acetic acid (30 ml) are added acetic anhydride (10 ml) and hydrogen peroxide (20 ml of a 30% solution). The mixture is kept at 0°C for 18 h and at 20 to 25°C for 1 h, and then poured into a solution of sodium perchlorate (0.1 mol) in water (200 ml). The resulting precipitate is filtered, washed with water, dried in vacuum over phosphorus pentoxide, and dissolved in dry acetonitrile (50 ml). To the solution cooled to 0°C is added sodium methoxide (0.011 mol) in methanol (0.5 ml), the solvent evaporated in vacuum, and the crude product purified by crystallization.

2,3-Dimethyl-4,6-dioxo-5-triphenylphosphoranylidene-1,4,5,6-tetrahydropyrimidine (10a):

The yield of the crude product is 58% (Method A) and 39% (Method B). Compound **10a** could not be obtained in analytically pure form. For chemical analysis, it was treated with an equimolar amount of perchloric acid (a 7% aqueous solution), filtered, and crystallized from ethanol to give **10a**·$HClO_4$. Yield 80%, mp 209-211°C. IR: 1700 (C=O), 3340 (N-H) cm^{-1}. ^1H NMR (DMSO-d_6): 2.55 (s, C(2)-CH_3), 3.23 (s, NCH_3), 7.4-7.9 (m, $3C_6H_5$). (Found: C, 57.35; H, 4.43; Cl, 7.11; N, 5.71; P, 6.18. Calc for $C_{24}H_{22}ClN_2O_6P$ (MW 500.86): C, 57.55; H, 4.43; Cl, 7.08; N, 5.59; P, 6.18%).

3-Methyl-4,6-dioxo-2-phenyl-5-triphenylphosphoranylidene-1,4,5,6-tetrahydropyrimidine (10b):

Yield 76% (Method A) and 41% (Method B), mp 239-241°C (from ethanol). IR: no intense absorption in the region of 1620-2300 cm^{-1}. UV (ε, CH_3CN): 227(4.43), 244(4.25), 262(4.21), 268(4.23), 274(4.15), 320(3.79) nm. ^1H NMR ($CDCl_3$): 3.52 (s, NCH_3), 7.2-8.6 (m, $4C_6H_5$). (Found: C, 75.23; H, 4.99; N, 5.98; P, 6.72. Calc for $C_{29}H_{23}N_2O_2P$ (MW 462.48): C, 75.32; H, 5.01; N, 6.06; P, 6.70%). Samples of compound **10b** obtained by methods A and B show no depression of mixed melting point. Their IR, UV, and ^1H NMR spectra are also identical.

2-R-6-Methylthio-4-oxo-5-triphenylphosphoranylidene-4,5-dihydropyrimidines (11a,b):

General procedure. To a solution of **8a** or **8b** (0.01 mol) in methylene dichloride (50 ml) is added methyl iodide (0.011 mol), the mixture is allowed to stand at 20 to 25°C for 12 h, after which the volatiles are removed in vacuum. To the residue preliminarily dissolved in methanol (50 ml) is added a solution of sodium methoxide (0.011 mol) in methanol (0.5 ml). After keeping the mixture at 20 to 25°C for 4 h, methanol is evaporated in vacuum and the residue washed with water, purified by crystallization, and thoroughly dried at 100 to 120°C for 3 to 4 h.

2-Methyl-6-methylthio-4-oxo-5-triphenylphosphoranylidene-4,5-dihydropyrimidine (11a):

Yield 94%, mp 245-247°C (from acetonitrile). IR: no intense absorption in the region of 1620-2300 cm^{-1}. ^1H NMR ($CDCl_3$): 2.28 (s, C(2)-CH_3), 2.43 (s, SCH_3), 7.27-7.95 (m, $3C_6H_5$). (Found: C, 69.28; H, 5.16; P,

7.51; S, 7.79. Calc for $C_{24}H_{21}N_2OPS$ (MW 416.48): C, 69.21; H, 5.08; P, 7.44; S, 7.70%). A thoroughly dried sample of compound **11a** prepared by the general procedure was found to be unsuitable for X-ray diffraction analysis. An appropriate sample in the form of solvate **11a**·CH_3CN·H_2O was obtained by dissolving one gram of wet **11a** in acetonitrile (15 ml) on heating and, after 12 h, the crystals formed are carefully filtered off and dried at 20°C (10 mmHg) for 1 h. Mp 245-247°C. (Found: C, 65.63; H, 5.49; P, 6.56; S, 6.78. Calc for $C_{24}H_{21}N_2OPS$·CH_3CN·H_2O (MW 475.55): C, 65.67; H, 5.51; P, 6.51; S, 6.74%).

6-Methylthio-4-oxo-2-phenyl-5-triphenylphosphoranylidene-4,5-dihydropyrimidine (11b):

Yield 93%, mp 283-285°C (from acetonitrile). (Found: N, 5.79; P, 6.51; S, 6.75. Calc for $C_{29}H_{23}N_2OPS$ (MW 478.56): N, 5.85; P, 6.47; S, 6.70%).

6-Methylthio-2-phenyl-4-thioxo-5-triphenylphosphoranylidene-4,5-dihydropyrimidine (12):

To a solution of **9** (0.01 mol) in methylene dichloride (20 ml) is added methyl iodide (0.011 mol) and the mixture is allowed to stand at 20 to 25°C for 4 h. After evaporation of the solvent in vacuum and dissolving the residue in absolute methanol, sodium methoxide (0.011 mol) in methanol (0.5 ml) is added, the precipitate filtered, washed with water, and crystallized from dimethylformamide. Yield 72%, mp 279-281°C. ^1H NMR ($CDCl_3$): 2.41 (s, SCH_3), 7.3-8.6 (m, $4C_6H_5$). (Found: N, 5.90; P, 6.10; S, 12.73. Calc for $C_{29}H_{23}N_2PS_2$ (MW 494.60): N, 5.66; P, 6.26; S, 12.97%).

1-Alkyl-2-methyl(phenyl)-4-methylthio-6-oxo-1,6-dihydropyrimidin-5-yl-triphenylphosphonium iodides (13a-c):

General procedure. To a solution of **11a** or **11b** (0.01 mol) in methylene dichloride (25 ml) is added the appropriate alkyl iodide (0.011 mol) and the reaction mixture is kept at 20 to 25°C for 6 h. After evaporation of the solvent in vacuum, the product is crystallized from ethanol.

1,2-Dimethyl-4-methylthio-6-oxo-1,6-dihydropyrimidin-5-yl-triphenylphosphonium iodide (13a):

Yield 88%, mp 165-167°C. (Found: P, 5.42; S, 5.58. Calc for $C_{25}H_{24}IN_2OPS$ (MW 558.42): P, 5.55; S, 5.74%). The general procedure failed to give a crystalline sample of **13a** suitable for X-ray diffraction measurements. The problem was eliminated by substituting the perchlorate anion for a iodide counterion in the compound (see the procedure for preparation of **13d**).

1-Methyl-4-methylthio-6-oxo-2-phenyl-1,6-dihydropyrimidin-5-yl-triphenylphosphonium iodide (13b):

Yield 95%, mp 259-261°. ^1H NMR ($CDCl_3$): 2.44 (s, SCH_3), 3.49 (s, NCH_3), 7.5-8.0 (m, $4C_6H_5$). (Found: I, 19.79; P, 4.82; S, 5.05. Calc for $C_{30}H_{26}IN_2OPS$ (MW 620.49): I, 20.05; P, 4.99; S, 5.17%).

1-Ethyl-4-methylthio-6-oxo-2-phenyl-1,6-dihydropyrimidin-5-yl-triphenylphosphonium iodide (13c): Yield 96%, mp 159-161°. IR: 1655 (C=O) cm^{-1}. (Found: I, 19.77; P, 4.72; S, 4.98. Calc for $C_{31}H_{28}IN_2OPS$ (MW 634.51): I, 20.00; P, 4.88; S, 5.05%).

1,2-Dimethyl-4-methylthio-6-oxo-1,6-dihydropyrimidin-5-yl-triphenylphosphonium perchlorate (13d): To a solution of **13a** (0.002 mol) in ethanol (15 ml) is added a saturated aqueous solution of sodium perchlorate (10 ml), the precipitate formed is filtered and crystallized from ethanol. Yield 94%, mp 248-251°. IR: 1637 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): 2.38 (s, C(2)-CH_3), 2.73 (s, SCH_3), 3.49 (s, NCH_3), 7.60-7.90 (m, $3C_6H_5$). (Found: C, 58.38; H, 4.75; P, 6.12. Calc for $C_{25}H_{24}ClN_2O_5PS$ (MW 514.97): C, 58.31; H, 4.70; P, 6.01%).

1-Alkyl-2-methyl(phenyl)-4-methylthio-6-oxo-1,6-dihydropyrimidines (14a-c):

General procedure. To a suspension of phosphonium salt **13a-c** (0.001 mol) in ethanol (5 ml) is added a solution of sodium hydroxide (0.002 mol) in water (0.5 ml). The mixture is refluxed for 3 h, the solvent removed in vacuum, the residue extracted with diethyl ether (2 x 10 ml), and the extract evaporated in vacuum to give the product, which is further purified by crystallization from ethanol.

1,2-Dimethyl-4-methylthio-6-oxo-1,6-dihydropyrimidine (14a):

Yield 35%, mp 68-69°C. ^1H NMR ($CDCl_3$): 1.54 (s, C(2)-CH_3), 1.60 (s, SCH_3), 2.58 (s, NCH_3), 5.92 (s, C(5)-H). (Found: C, 49.28; H, 5.88; N, 16.38; S, 18.67. Calc for $C_7H_{10}N_2OS$ (MW 170.24): C, 49.39; H, 5.92; N, 16.45; S, 18.84%).

1-Methyl-4-methylthio-6-oxo-2-phenyl-1,6-dihydropyrimidine (14b):

Yield 70%, mp 151-153°C. IR: 1650 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): 2.43 (s, SCH_3), 3.41 (s, NCH_3), 6.23 (s, C(5)-H), 7.51 (s, C_6H_5). (Found: N, 12.05; S, 13.80. Calc for $C_{12}H_{12}N_2OS$ (MW 232.30): N, 12.05; S, 13.80%).

1-Ethyl-4-methylthio-6-oxo-2-phenyl-1,6-dihydropyrimidine (14c):

Yield 55%, mp 45°C. ^1H NMR ($CDCl_3$): 1.44 (t, CH_3CH_2), 2.63 (s, SCH_3), 4.52 (q, CH_3CH_2), 6.46 (s, C(5)-H), 7.3-7.7 (m, C_6H_5). (Found: N, 11.31; S, 12.93. Calc for $C_{13}H_{14}N_2OS$ (MW 243.33): N, 11.37; S, 13.02%).

6-Alkylthio-4-methylthio-2-phenylpyrimidin-5-yl-triphenylphosphonium iodides (15b,c):

General procedure. To a solution of **12** (0.001 mol) in methylene dichloride (5 ml) is added the appropriate alkyl iodide (0.0011 mol). After keeping the mixture at 20 to 25°C for 6 h, the solvent is evaporated in vacuum giving the product, which is further purified by crystallization from ethanol.

4,6-Di(methylthio)-2-phenylpyrimidin-5-yl-triphenylphosphonium iodide (15b):

Yield 85%, mp 257-259°C. (Found: I, 19.75; P, 4.89; S, 9.95. Calc for $C_{30}H_{26}IN_2PS_2$ (MW 636.35): I, 19.94; P, 4.87; S, 10.07%).

6-Ethylthio-4-methylthio-2-phenylpyrimidin-5-yl-triphenylphosphonium iodide (15c):

Yield 82%, mp 224-226°C. (Found: I, 19.28; P, 4.74; S, 9.82. Calc for $C_{31}H_{28}IN_2PS_2$ (MW 650.57): I, 19.51; P, 4.76; S, 9.86%).

6-Alkylthio-4-methylthio-2-phenylpyrimidines (16b,c):

General procedure. To a suspension of phosphonium salt **15b** or **15c** (0.001 mol) in ethanol (5 ml) is added a solution of sodium hydroxide (0.002 mol) in water (0.5 ml). The reaction mixture is refluxed for 15 h, the solvents removed in vacuum, and the residue extracted with diethyl ether (2 x 10 ml). The extract is evaporated in vacuum giving the crude product, which is subjected further to crystallization from petroleum ether (bp 40-70°C).

4,6-Di(methylthio)-2-phenylpyrimidine (16b):

Yield 67%, mp 80-81°C, in agreement with literature[24]. ^{1}H NMR (acetone-d_6): 2.70 (s, $2SCH_3$), 7.17 (s, C(5)-H), 7.3-7.8 (m, 3H), 8.3-8.7 (m, 2H). (Found: N, 11.26; S, 25.79. Calc for $C_{12}H_{12}N_2S_2$ (MW 248.36): N, 11.28; S, 25.82%).

6-Ethylthio-4-methylthio-2-phenylpyrimidine (16c):

Yield 63%, light-yellow viscous oil, n_D^{20} 1.6562. ^{1}H NMR (acetone-d_6): 1.46 (t, CH_3CH_2), 2.60 (s, SCH_3), 3.32 (q, CH_3CH_2), 7.12 (s, C(5)-H), 7.3-7.8 (m, 3H), 8.3-8.7 (m, 2H). (Found: N, 10.48; S, 24.23. Calc for $C_{13}H_{14}N_2S_2$ (MW 262.39): N, 10.67; S, 24.44%).

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