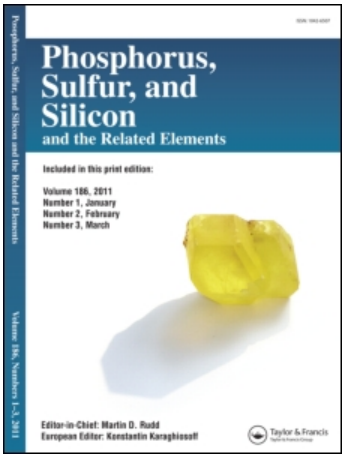

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REACTIONS OF URACILS, 18[1]: REACTION OF 5-FORMYL-1,3-DIMETHYL-BARBITURIC ACID AND 5-FORMYL-1,3,6-TRIMETHYLURACIL WITH ETHOXYCARBONYL-METHYLENETRIPHENYLPHOSPHORANE

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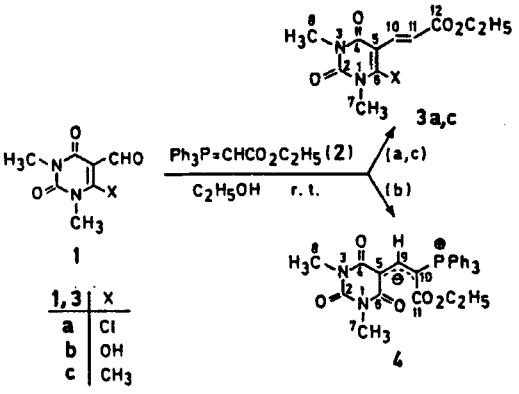
Ethoxycarbonylmethylenetriphenylphosphorane (**2**) reacts with 5-formyl-1,3,6-trimethyluracil (**1c**) in the expected way to afford the acrylate **3c**, while with 5-formyl-1,3-dimethylbarbituric acid (**1b**) a novel phosphorus ylide/phosphorane **4** is obtained (X-ray analysis). The temperature dependent NMR spectra and the mechanism of formation are discussed.

Key words: 5-Formyl-1,3-dimethylbarbituric acid; 5-formyl-1,3,6-trimethyluracil; Wittig reaction; phosphorus ylide; ethoxycarbonylmethylenetriphenylphosphorane.

Recently, we have reported on a novel series of 6-chloro- and 6-amino-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-yl acrylates[2] showing their synthetic utility in building of novel uracils[3] as well as fused ring systems.[4,5] Furthermore, the reaction of 6-chloro-5-formyl-1,3-dimethyluracil (**1a**) with ethoxycarbonylmethylenetriphenylphosphorane (**2**) results in a facile preparation of the 5-pyrimidine acrylate derivative **3a**, a key intermediate for subsequent transformations.

Now, we want to report on further observations, when 5-formyl-1,3-dimethylbarbituric acid (**1b**) and 5-formyl-1,3,6-trimethyluracil (**1c**) are reacted with phosphorane **2**, since Wittig reactions of **1b** or other 5-formylbarbituric acids have not yet been described.

When **1b** was treated with phosphorane **2** in ethanol at room temperature for 72 h, instead of the expected acrylate, the novel phosphorus ylide **4** is formed in 28% yield:



1,3	X
a	Cl
b	OH
c	CH_3

*Dedicated to Professor *Karl-Heinz Büchel* on the occasion of his 60th birthday.

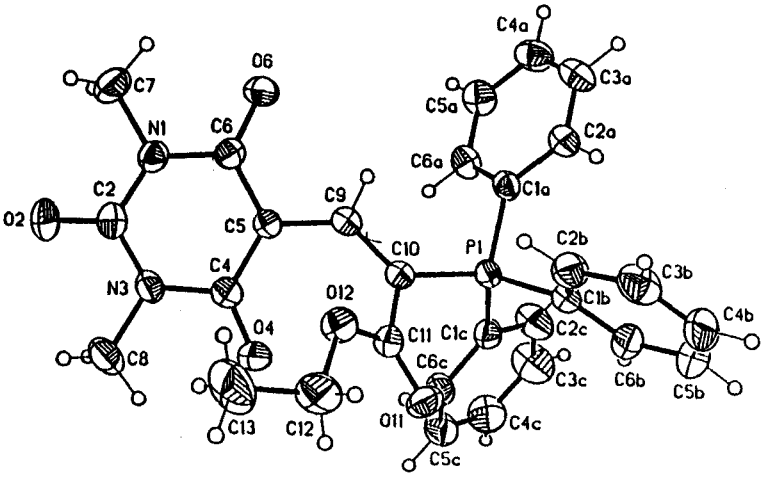


FIGURE 1 Crystal structure of **4**. Selected bond distances [Å] and angles [°]: C(2)—O(2) 1.225(3), C(4)—O(4) 1.233(3), C(6)—O(6) 1.236(3), C(5)—C(9) 1.414(3), C(9)—C(10) 1.379(4), C(10)—C(11) 1.470(3), C(10)—P(1) 1.774(2); C(4)—C(5)—C(9) 121.9(2), C(5)—C(9)—C(10) 129.7(2), C(9)—C(10)—P(1) 120.0(2), C(9)—C(10)—C(11) 126.2(2).

TABLE I

Crystal and structure data of **4**

Formula	$C_{29}H_{27}N_2O_5P$
Mol. mass	514.5
Crystal size [mm^3]	0.4 x 0.5 x 0.5
Color	light yellow
Crystal system	monoclinic
Space group	$P2_1/n$
a [Å]	9.744(2)
b [Å]	25.171(4)
c [Å]	10.899(3)
ß [°]	94.93(2)
V [nm^3]	2.661
d_x [$g \cdot cm^{-3}$]	1.28
Z	4
T [°C]	25
Final high in $\Delta\rho$ - map[$Å^{-3}$]	0.50
μ (Mo-K_α) [mm^{-1}]	0.14
λ [Å]	0.71069
Scan range	$2\Theta_{max} = 45°$
R	0.043
R_w	0.045

TABLE II

Bond lengths (Å) of **4**

N(1)-C(2)	1.379(3)	N(1)-C(6)	1.396(3)
N(1)-C(7)	1.470(4)	C(2)-N(3)	1.376(3)
C(2)-O(2)	1.225(3)	N(3)-C(4)	1.411(3)
N(3)-C(8)	1.469(4)	C(4)-C(5)	1.434(3)
C(4)-O(4)	1.233(3)	C(5)-C(6)	1.437(4)
C(5)-C(9)	1.414(3)	C(6)-O(6)	1.236(3)
C(9)-C(10)	1.379(4)	C(10)-C(11)	1.470(3)
C(10)-P(1)	1.774(2)	C(11)-O(11)	1.211(3)
C(11)-O(12)	1.345(3)	O(12)-C(12)	1.450(4)
C(12)-C(13)	1.449(5)	P(1)-C(1a)	1.805(2)
P(1)-C(1b)	1.802(3)	P(1)-C(1c)	1.809(3)
C(1a)-C(2a)	1.391(4)	C(1a)-C(6a)	1.398(4)
C(2a)-C(3a)	1.375(4)	C(3a)-C(4a)	1.380(5)
C(4a)-C(5a)	1.382(4)	C(5a)-C(6a)	1.385(4)
C(1b)-C(2b)	1.386(4)	C(1b)-C(6b)	1.390(4)
C(2b)-C(3b)	1.386(4)	C(3b)-C(4b)	1.375(5)
C(4b)-C(5b)	1.354(5)	C(5b)-C(6b)	1.389(4)
C(1c)-C(2c)	1.390(4)	C(1c)-C(6c)	1.384(4)
C(2c)-C(3c)	1.382(5)	C(3c)-C(4c)	1.380(5)
C(4c)-C(5c)	1.368(5)	C(5c)-C(6c)	1.380(4)

TABLE III

Bond angles (°) of **4**

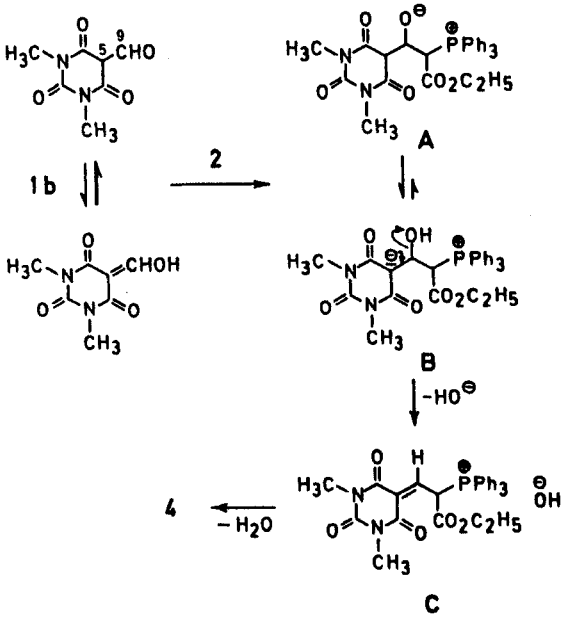
C(2)-N(1)-C(6)	124.2(2)	C(2)-N(1)-C(7)	116.7(2)
C(6)-N(1)-C(7)	119.0(2)	N(1)-C(2)-N(3)	117.0(2)
N(1)-C(2)-O(2)	121.3(2)	N(3)-C(2)-O(2)	121.8(2)
C(2)-N(3)-C(4)	124.8(2)	C(2)-N(3)-C(8)	117.1(2)
C(4)-N(3)-C(8)	118.1(2)	N(3)-C(4)-C(5)	116.1(2)
N(3)-C(4)-O(4)	118.0(2)	C(5)-C(4)-O(4)	125.8(2)
C(4)-C(5)-C(6)	120.7(2)	C(4)-C(5)-C(9)	121.9(2)
C(6)-C(5)-C(9)	116.4(2)	N(1)-C(6)-C(5)	117.2(2)
N(1)-C(6)-O(6)	118.9(2)	C(5)-C(6)-O(6)	123.9(2)
C(5)-C(9)-C(10)	129.7(2)	C(9)-C(10)-C(11)	126.2(2)
C(9)-C(10)-P(1)	120.0(2)	C(11)-C(10)-P(1)	113.8(2)
C(10)-C(11)-O(11)	123.5(2)	C(10)-C(11)-O(12)	112.4(2)
O(11)-C(11)-O(12)	123.8(2)	C(11)-O(12)-C(12)	116.5(2)
O(12)-C(12)-C(13)	110.4(3)	C(10)-P(1)-C(1a)	110.7(1)
C(10)-P(1)-C(1b)	110.6(1)	C(1a)-P(1)-C(1b)	107.8(1)
C(10)-P(1)-C(1c)	111.9(1)	C(1a)-P(1)-C(1c)	106.3(1)
C(1b)-P(1)-C(1c)	109.4(1)	P(1)-C(1a)-C(2a)	120.8(2)
P(1)-C(1a)-C(6a)	120.0(2)	C(2a)-C(1a)-C(6a)	119.2(2)
C(1a)-C(2a)-C(3a)	120.3(3)	C(2a)-C(3a)-C(4a)	120.2(3)
C(3a)-C(4a)-C(5a)	120.5(3)	C(4a)-C(5a)-C(6a)	119.6(3)
C(1a)-C(6a)-C(5a)	120.2(2)	P(1)-C(1b)-C(2b)	119.5(2)
P(1)-C(1b)-C(6b)	121.2(2)	C(2b)-C(1b)-C(6b)	119.2(2)
C(1b)-C(2b)-C(3b)	120.2(3)	C(2b)-C(3b)-C(4b)	119.8(3)
C(3b)-C(4b)-C(5b)	120.5(3)	C(4b)-C(5b)-C(6b)	120.7(3)
C(1b)-C(6b)-C(5b)	119.5(3)	P(1)-C(1c)-C(2c)	119.8(2)
P(1)-C(1c)-C(6c)	121.0(2)	C(2c)-C(1c)-C(6c)	119.2(3)
C(1c)-C(2c)-C(3c)	120.1(3)	C(2c)-C(3c)-C(4c)	119.9(3)
C(3c)-C(4c)-C(5c)	120.1(3)	C(4c)-C(5c)-C(6c)	120.3(3)
C(1c)-C(6c)-C(5c)	120.3(3)		

The structure of **4** was unambiguously established by single crystal X-ray analysis (cf. Figure 1) and the information obtained suggests a delocalization of the negative charge over C-5, 9, 10, while the positive charge can be localized at the phosphorus atom.

In the ^{1}H NMR spectrum of **4** at room temperature ($CDCl_3$ or [D_6]DMSO), two sets of ester and N—CH_3 signals were found (intensity ratio 5.5) owing to a restricted rotation about the C-19,10 bond, while at 130°C ([D_6]DMSO) only one isomer could be detected, and, accordingly, two signals appeared (intensity ratio *ca.* 6) at room temperature in the ^{31}P NMR spectrum. However, only one set of signals could be observed in the ^{13}C NMR spectrum, where the value of the coupling constant between 9-H and C-11 ($^3J_{C-H}$ = 12 Hz) supports a *trans* arrangement of 9-H and the C-10,11 bond.[6]

Scheme II shows a working hypothesis for the formation of **4**. The Wittig reagent **2** adds to the activated 5,6-double bond (cf. lit.[7]) of the hydroxymethylene tautomer of **1b** to give intermediate **B**; an alternative pathway involves firstly intermediate **A**. Next, splitting of OH^- from **B** and subsequent elimination of H_2O from **C** affords the novel phosphorane **4**. A similar approach is known for the reaction of diethyl ethoxymethylenemalonates with cyanomethylenetriphenylphosphorane.[8] But, obviously, there still exists an important difference to this latter reaction. In the case of **1b**, the hydroxymethylene group is capable of tautomerism with the aldehyde form, and, consequently it should smoothly undergo Wittig olefination.[9] In ethoxymethylenemalonates, such an equilibrium is *ab ovo* excluded.

In a recent communication,[10] it has been stated that 5-pyrimidine acrylate **3c** could not be isolated in pure state after reacting **1c** with Wittig reagent **2** in benzene.



SCHEME II

However, in our experiment employing ethanol as solvent, **3c** could be successfully isolated and unambiguously characterized by its analytical data. But neither in ethanol nor in acetonitrile a phosphorane analogous to **4** has been detected. Thus, this unexpected formation of ylide **4** seems to be limited to aldehydes which are capable of a tautomeric equilibrium with their hydroxymethylene form, and bearing electron withdrawing substituents. Further work in this field is in progress.

EXPERIMENTAL

IR: Perkin-Elmer 157-G. ^1H and ^{13}C NMR: Bruker WH-90, AC-200 and AM-400; ^{31}P NMR: Varian CFT-20 (vs. 85% H_3PO_4). MS: MS-30 and MS-50 of Kratos (A.E.I.). Melting points are uncorrected. Elemental analyses: Analytical Department of our Institute.

Compounds **1b**[11] and **1c**[12] were prepared according to the literature procedures.

Reaction of 5-formyl-1,3-dimethylbarbituric acid (**1b**) *with phosphorane* **2**: *Synthesis of 2-ethoxycarbonyl-3-[(1,3-dimethyl-2,4,6(1H, 3H, 5H)-trioxopyrimidin-5-yl)-2-propen-1-ylidene]triphenylphosphorane* **4**: To a stirred suspension of 0.83 g (4.5 mmol) of **1b** in anhydrous ethanol are added in an argon atmosphere at room temperature 1.74 g (5.0 mmol) of **2**. The mixture is stirred at room temperature for 72 h, then filtered. The yellow crystals are collected, recrystallized from ethanol and dried at 80°C/0.5 Torr to give 0.65 g (28%) of **4**; m.p. 251–252°C. IR(KBr): ν = 1701, 1674, 1624 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$; the signals of minor components underlined): δ = 0.89, 0.93 (3H, t, $CH_2\underline{CH_3}$), 3.25, 2.91 (6H, br. s, 2 N—CH_3), 3.95, 3.86 (4H, q, $\underline{CH_2}CH_3$), 7.48 (1H, d, $^3J_{P-H}$ = 21.1 Hz, 9-H), 7.55–7.75 ppm (15H, m, H_{ar}). ^{13}C NMR (22.6 MHz, $CDCl_3$): δ = 13.9 ($CH_2\underline{CH_3}$), 27.7 (C-7,8), 60.3 ($\underline{CH_2}CH_3$), 86.0 (d, J_{P-C} = 103.6 Hz, C-10), 98.2 (d, J_{P-C} = 15.8 Hz, C-5), 121.6 (d, J_{P-C} = 91.3 Hz, C_{ar}-1'), 129.5 (d, J_{PC} = 12.7 Hz, C_{ar}-3',5'), 133.9 (d, J_{P-C} = 1 Hz, C_{ar}-4'), 134.2 (d, J_{P-C} = 10.1 Hz, C_{ar}-2',6'), 152.9 (C-2), 154.0 (d, J_{P-C} = 14.3 Hz, C-9), 162.7 (C-4,6), 167.2 ppm (d, J_{P-C} = 16.3 Hz, C-11). ^{31}P NMR (32.38 MHz, $CDCl_3$): δ = 26.6, 17.2 ppm. MS (70 eV): *m/z* 514 (M^+).

$C_{29}H_{27}N_2O_5P$ (514.5)	Calcd.	C 67.69	H 5.29	N 5.44
	Found	C 67.41	H 5.20	N 5.32

E-Ethyl[3-(1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-yl)-acrylate] (**3c**): To a stirred suspension of 0.45 g (2.5 mmol) of **1c** in 5 ml of ethanol a solution of 0.87 g (2.5 mmol) of **2** in 4 ml of ethanol is added at room temperature and in an argon atmosphere. The mixture is stirred for 24 h, then filtered. The white crystals are recrystallized from ethanol to give 0.36 g (57%) of **3c**, m.p. 158–159°C. IR(KBr): ν = 1705, 1695, 1660 cm^{-1} (CO). ^1H NMR (90 MHz, $CDCl_3$): δ = 1.20 (3H, t, $CH_2\underline{CH_3}$), 2.40 (3H, s, 9-CH_3), 3.42 (3H, s, 8-CH_3), 3.58 (3H, s, 7-CH_3), 4.10 (2H, q, $\underline{CH_2}CH_3$), 7.05 (1H, d, J = 16 Hz, 11-H), 7.60 ppm (1H, d, J = 16 Hz, 10-H). ^{13}C NMR (22.6 MHz, $CDCl_3$): δ = 14.3 ($CH_2\underline{CH_3}$), 16.9 (C-9), 28.3 (C-8), 32.8 (C-7), 60.3 ($\underline{CH_2}Ch_3$), 107.0 (C-5), 121.1 (C-11), 135.5 (C-10), 151.4 (C-4), 152.9 (C-6), 160.9 (C-2), 168.1 ppm (C-12). MS (70 eV): *m/z* 252 (M^+).

$C_{12}H_{16}N_2O_4$ (252.3)	Calcd.	C 57.13	H 6.39	N 11.11
	Found	C 56.99	H 6.39	N 10.90

X-ray analysis of **4**: A single crystal (obtained from dichloromethane/hexane) was chosen for this investigation: 5838 reflections ($2\theta_{max}$ = 45°) were measured on a Nicolet R3m four-circle diffractometer using graphite-monochromated Mo-Kα radiation. Table I contains all crystal data and further details of the structure analysis. The ω-scan mode was used (scan range 1.2°). From 3481 symmetry independent reflections 2758 reflections with $|F| > 4\sigma(F)$ were used for the structure solution (Direct Methods) and refinement (334 parameters), nonhydrogen atoms were refined anisotropically ("blocked cascade" refinement), H-atoms localized by difference electron density determination and refined using a 'riding' model, R = 0.043 (R_w = 0.045, $\omega^{-1} = \sigma^2(F) + 0.0005\,F^2$).

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