Reactions of Uracils. 6.[1,2] New Ring Transformations of 6-Aminouracils with Acetylenedicarboxylates to Pyridinedionates and Pyrrolo[3,4-*c*]pyridines. Some Revised Constitutions

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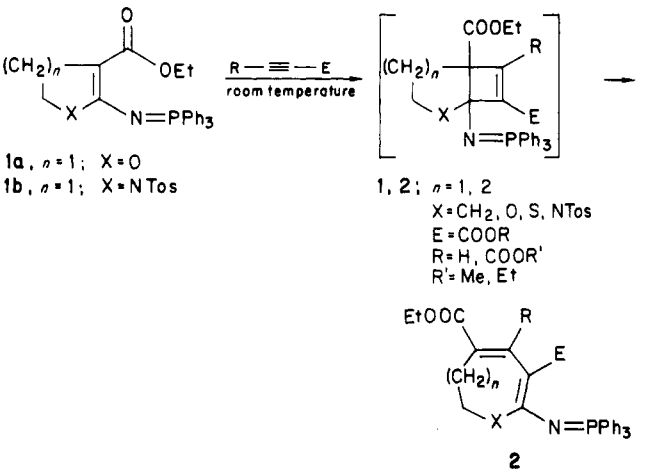
Treatment of 6-[(triphenylphosphoranylidene)amino]-1,3-dimethyluracils **8** with dialkyl acetylenedicarboxylates in aprotic solvents affords zwitterionic pyridinedionates **12**, involving a novel ring transformation reaction, via cleaving attack of a terminal carbanion to the 2-carbonyl of the uracil. In protic solvents **12** undergo a smooth heterocyclization reaction to give the pyrrolo[3,4-*c*]pyridines **14**. The structures of **12b** and **14b** have been established by single-crystal X-ray diffraction. By spectroscopic comparison as well as by independent syntheses **12** proved to be closely related (phosphorylated) analogues of previously reported "ureas **17** and **18**", while **13** was identical with the "5-propynoyluracil **15**". Catalytic hydrogenation of **13a** gave carbinol **20**, which proved by means of ^1H (H–D exchange) and ^{13}C NMR to be identical with "*cis*-olefin **19**".

Most studies concerning the cycloaddition tendency of the 5,6-double bond of uracils have dealt with photodimerization reactions,[4] with photochemical (2 + 2)-cycloadditions,[5] and more recently with (2 + 2 + 2)-photocycloadditions of acetylenic triple bonds leading to bicyclo[4.2.0]hexane systems.[6] Furthermore, the acetone-sensitized photocycloaddition of uracil and its derivatives with alkynes affords a 2,4-diazabicyclo[4.2.0]-oct-7-ene-3,5-dione, with subsequent ring-expansion reaction to 1,3-diaza-5,7-cyclooctadiene-2,4-dione by silylation and treatment with silica gel.[7] Another novel and unusual cyclization mode yielding bridged 1,2,5,6-tetrazocanes with uracil and urazole bridging units has just been reported.[1]

The forementioned two-carbon ring-expansion procedure, as well as a general and versatile cycloaddition–ring expansion sequence found for partially saturated (2-

Scheme I



Scheme II

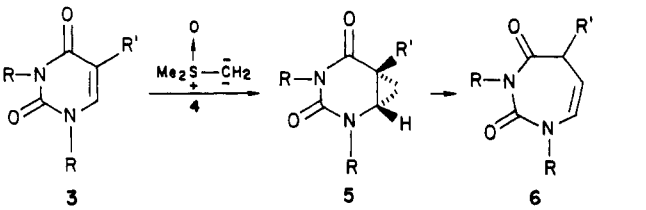


Table I. Comparison of ^{13}C NMR Data (δ) of 1 and 8

compd	C-2	C-3
1a	166.80	80.22
1b	155.05	84.84
compd	C-6	C-5
8a	157.29	84.52
8b	156.23	92.57

cycloalkylimino)-, (2-thienylimino)-, (2-furylimino)-, (2-pyrrolylimino)-, and (2-thiopyranimino)triphenylphosphoranes **1** affording cyclooctadienes and dihydrothiepins, -oxepins, -azepines, and -2*H*-thiocins **2**, respectively (cf. Scheme I),[2,8,9] led us to try analogously a thermal

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(2) Part 8 of the series: Dihalogenotriphenylphosphoranes in Heterocyclic Synthesis. Part 7: Wamhoff, H.; Hendrikx, G. *Chem. Ber.* **1985**, *118*, 863.

(3) Based in part on Diplomarbeit and Dissertation W. Schupp, Universität. Bonn, 1983–1985.

(4) For reviews in this area, see: (a) Burr, J. R. *Adv. Photochem.* **1968**, *6*, 193. (b) McLaren, A. D.; Shugar, D. "Photochemistry of Proteins and Nucleic Acids"; Macmillan: New York, 1961; pp 162–220. (c) Fisher, G. J.; Johns, H. E. In "Photochemistry and Photobiology of Nucleic Acids"; Wang, S. Y., Ed.; Academic Press: New York, 1976; Vol. I, pp 226–289. (d) Wamhoff, H. *Kem. Kozl.* **1983**, *59*, 251; *Chem. Abstr.* **1984**, *102*, 23706y. (e) Kleopfer, R.; Morrison, H. *J. Am. Chem. Soc.* **1972**, *94*, 255.

(5) For leading references, see: (a) Krajewskaja, E.; Shugar, D. *Science (Washington, D.C.)* **1971**, *173*, 435. (b) Helene, C.; Brun, F. *Photochem. Photobiol.* **1970**, *11*, 77. (c) Beugelmans, R.; Furrey, J. L.; Gero, S.; Le Goff, M.; Mercier, D.; Ratovelomanana, V.; Janot, M. *C. R. Seances Acad. Sci., Ser. C* **1972**, *274*, 882. (d) Hyatt, J. A.; Swenton, J. S. *J. Am. Chem. Soc.* **1972**, *94*, 7605. (e) Szilágyi, G.; Wamhoff, H.; Sohár, P. *Chem. Ber.* **1974**, *107*, 1265. (f) Bergstrom, D. E.; Agosta, W. C. *Tetrahedron Lett.* **1974**, *1087*. (g) Swenton, J. S.; Hyatt, J. A.; Lisy, J. M.; Clardy, J. *J. Am. Chem.* Soc. **1974**, *96*, 4885. (h) Wexler, A.; Balchunis, R. J.; Swenton, J. S. *J. Chem. Soc., Chem. Commun.* **1975**, 601. (i) Varghese, A. J. *Photochem. Photobiol.* **1975**, *21*, 147. (j) Wexler, A.; Swenton, J. S. *J. Am. Chem. Soc.* **1976**, *98*, 1602. (k) Wexler, A.; Hyatt, J. A.; Reynolds, P. W.; Cotrell, C.; Swenton, J. S. *J. Am. Chem. Soc.* **1978**, *100*, 512. (l) Wamhoff, H. In "Steric Effects in Biomolecules"; Náray-Szábo, G., Ed.; Akadémiai Kiadó: Budapest, 1982; pp 195–211. (m) Chiba, T.; Takahashi, H.; Kato, T. *Heterocycles* **1982**, *19*, 703. (n) Szilágyi, G.; Wamhoff, H. *Angew. Chem.* **1983**, *95*, 156; *Angew. Chem. Suppl.* **1983**, 120; *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 157.

(6) Itoh, T.; Ogura, H.; Kawahara, N.; Watanabe, K. A. *Heterocycles* **1979**, *12*, 1175.

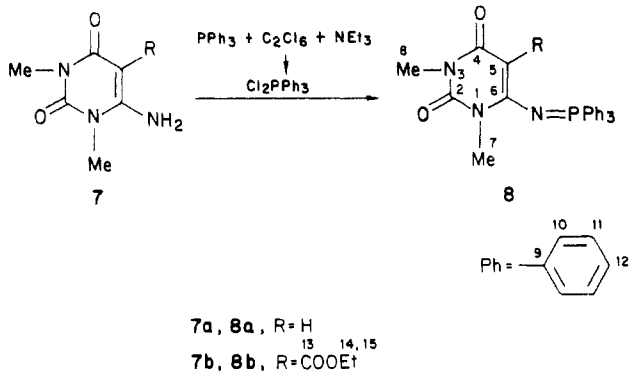
(7) Kaminski, V. V.; Comber, R. N.; Wexler, A. J.; Swenton, J. S. *J. Org. Chem.* **1983**, *48*, 2337.

(8) Wamhoff, H.; Haffmanns, G.; Schmidt, H. *Chem. Ber.* **1983**, *116*, 1691.

(9) (a) Wamhoff, H.; Haffmanns, G. *Chem. Ber.* **1984**, *117*, 585. (b) Wamhoff, H.; Böhle, A., manuscript in preparation.

0022-3263/86/1951-0149$01.50/0

Scheme III



7a, 8a, R = H
7b, 8b, R = ^{13}COO^{14,15}Et

polar (2 + 2)-cycloaddition of acetylenedicarboxylates with 6-[(triphenylphosphoranylidene)amino]uracils, which should give rise to two-carbon ring-expanded 2,4-dioxo-1,3-diazonine derivatives.

Thermal cycloadditions to the 5,6-double bond of uracils **3** so far are only known for carbenes (2 + 1 → 3) employing dimethyloxosulfonium methylide **4**, involving subsequent photoinduced ring enlargement of **5** to 1,3-diazepine-2,4-diones **6**[10] (cf. Scheme II). This work was prompted by cycloaddition of halocarbenes to yield 1,3-diazepines upon heating.[11] The reaction was furthermore extended to sulfonyl analogues of uracils,[12] while a photogenerated uracil-6-nitrene species inserts to give 1,3,5-triazepines.[13]

Results and Discussion

Calculations and PES spectra provide evidence that uracils and derivatives contain definite enamine functional subunits in their N-substituted 5,6-double bond region.[14] These findings are further supported by ^{13}C NMR comparison of the heterocyclic iminophosphoranes **1a,b**[2,9] and uracils **8a,b** (see Table I), the latter being easily obtained by phosphorylation[15] of **7**[16] with dichlorotriphenylphosphorane (Scheme III). The strong alternance of the ^{13}C NMR values both for C-2/C-3 in **1** and C-5/C-6 in **8** as reported for open-chain and cyclic enamines and enamino ketones[17] indicate a significant polarization much stronger than, e.g., in 1,3-dimethyluracil (C-5, δ 100.9; C-6, δ 143.2).[18]

Surprisingly, **8** upon treatment with dialkyl acetylenedicarboxylates in aprotic solvent gave neither the expected (2 + 2)-cycloadduct nor a ring-enlarged diazocine. Instead, unique heterocyclic transformation products **12** were isolated (Scheme IV). The structure of **12b** was established unambigously with the aid of single crystal X-ray diffraction analysis.

According to X-ray analysis **12b** in the solid state adopts a quasi-aromatic dioxopyridinedioate ring (planar, nearly identical bond lengths).[19] This can be explained in terms

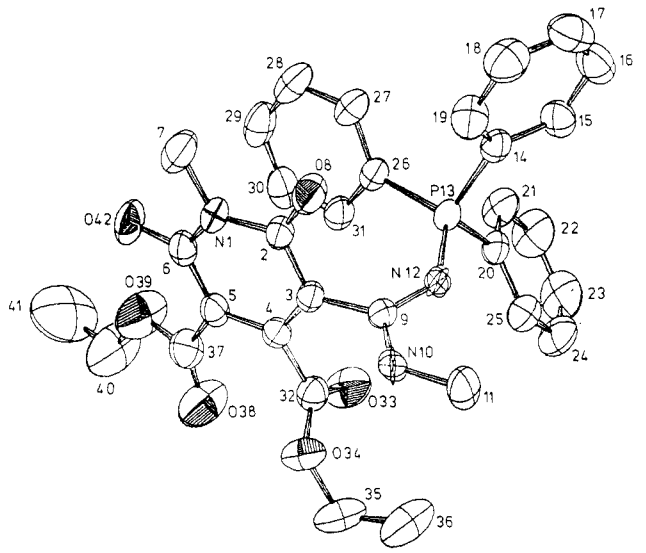


Figure 1. An ORTEP plot showing the structure of **12b** in the solid state from a single-crystal X-ray analysis.

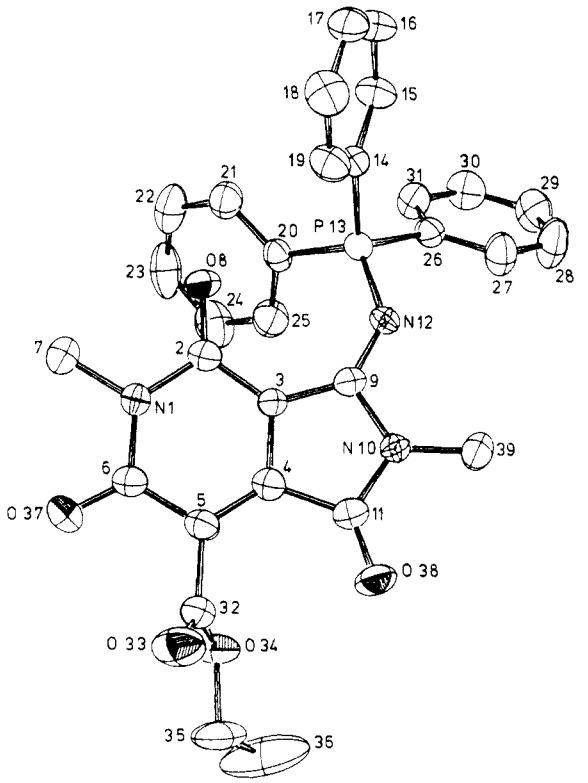


Figure 2. An ORTEP plot showing the structure of **14b** in the solid state from a single-crystal X-ray analysis.

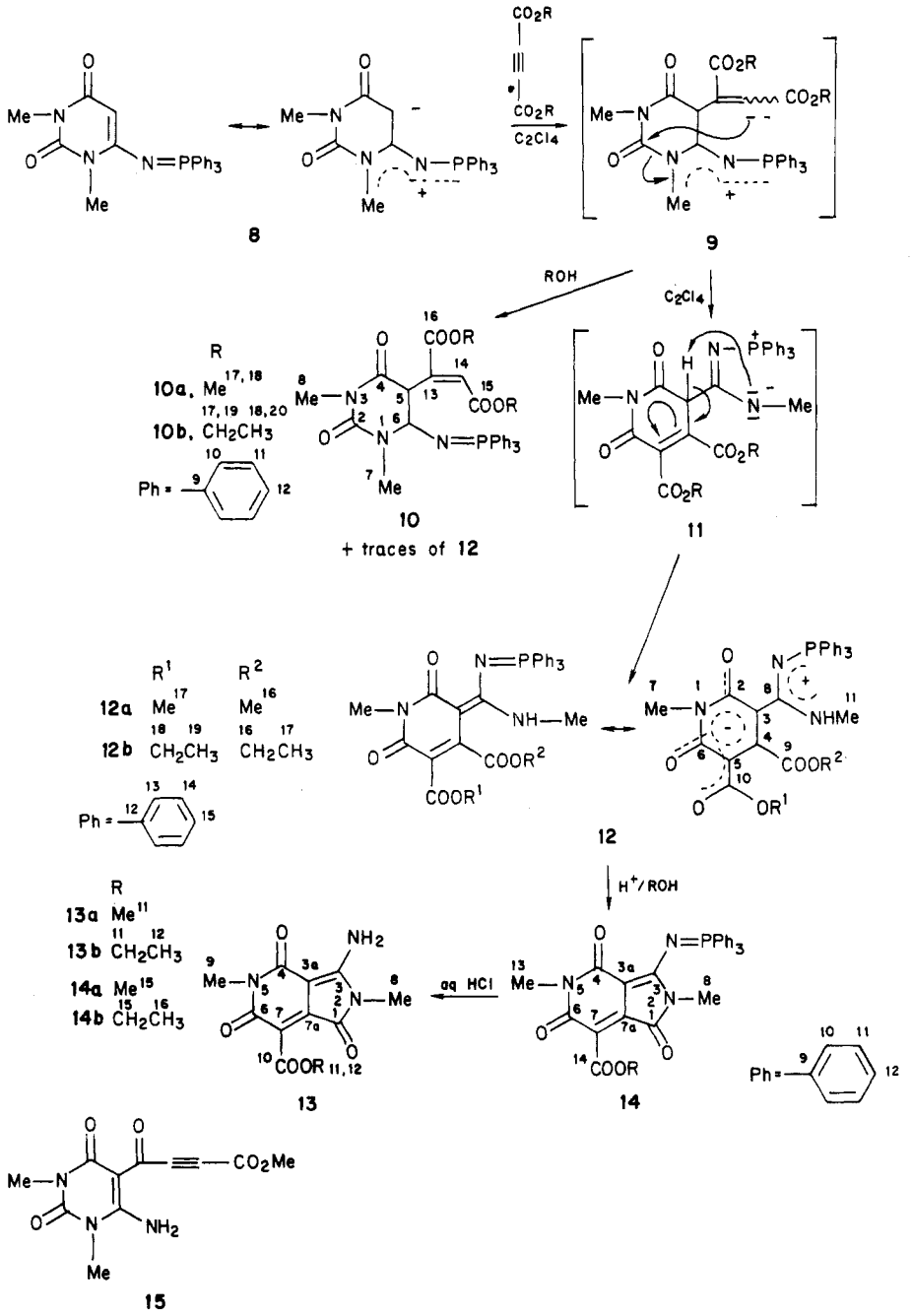
of a zwitterionic structure with an almost 90° twisted amidinium group as shown in formulae **12**. Structure **12** represents an unique heterocyclic zwitterionic form which in solution may be also depicted by a covalent canonical form. A stereoview and the numbering scheme of the molecule are shown in Figure 1.

Additionally, the ^{13}C NMR data of **12** are in excellent agreement with the constitutions revealing for C-3 and C-8 atypical longrange P–C coupling constants ($^{3}J_{P/C-3}$ = 7 Hz, $^{2}J_{P/C-8}$ = 6 Hz); the shift values indicate a well defined alternation (C-3, δ 101.25; C-4, δ 166.52) in accordance with

(10) Kunieda, T.; Witkop, B. *J. Am. Chem. Soc.* **1971**, *93*, 3478.
(11) Thiellier, H. P. M.; Koomen, G. J.; Pandit, U. K. *Heterocycles* **1976**, *5*, 19; *Tetrahedron* **1977**, *33*, 1493, 2603, 2609.
(12) Elguero, J.; Ochoa, C.; Stud, M. *Heterocycles* **1982**, *7*, 401.
(13) Senda, S.; Hirota, K.; Asao, T.; Maruhashi, K.; Kitamura, N. *Tetrahedron Lett.* **1978**, 1531.
(14) Lauer, G.; Schäfer, W.; Schweig, A. *Tetrahedron Lett.* **1975**, 3939.
(15) Appel, R.; Halstenberg, M. In "Organophosphorus Reagents in Organic Synthesis"; Cadogan, J. I. G., ed.; Academic Press: London, 1979; pp 378ff.
(16) (a) Papesch, A.; Schroeder, E. F. *J. Org. Chem.* **1951**, *16*, 1879. (b) Bernier, J. L.; Lefebvre, A.; Henichart, J.; Houssin, R.; Lespagnol, C. *Bull. Soc. Chim. Fr.* **1976**, *116*, 616.
(17) (a) Hickmott, P. W. *Tetrahedron* **1983**, *38*, 3363. (b) Tourwé, D.; Van Binst, G.; De Graaf, S. A. G.; Pandit, U. K. *Org. Magn. Reson.* **1975**, *7*, 433. (c) Ahmed, M. G.; Hickmott, P. W. *J. Chem. Soc., Perkin Trans 2* **1977**, 838.
(18) Cf.: Johnson, L. F.; Jankowski, W. C. "Carbon-13-NMR-Spectra"; Wiley-Interscience: New York, 1972; Spectrum No. 170.

(19) Typical bond lengths of the dioxopyridinedioate ring and of one ester group in **12b** are (in pm): N1–C2, 139.4 (3); C2–C3, 143.1 (4); C3–C4 136.9 (4); C4–C5, 140.4 (4); C5–C6, 142.9 (4); C6–N1, 138.9 (4); C6–O42, 123.8 (4); C2–O8, 123.1 (4); C5–C37, 146.2 (4); C37–O38, 118.4 (5).

Scheme IV



the formulated zwitterionic moiety.

These zwitterions **12** and especially the methyl derivative **12a** turned out to be unstable in protic solvents, smoothly converting to pyrrolo[3,4-*c*]pyridines **14**. This cyclization is already observed when dissolving **12** in alcohols. In order to get evidence that the zwitterionic molecule **12** is not reopened and/or rearranged during treatment with those protic solvents, the structure of **14b** was established by means of another single-crystal X-ray diffraction analysis (cf. Figure 2). According to X-ray analysis **14b** adopts a bicyclic system, where a pyrrole ring is fused with its C-3,4 moiety to plane c of the pyridine ring. As substituents are shown three C=O groups in positions 1,4, and 6, an ester function bound to C-7, and the iminophosphorane at C-3.[20]

14 possess an extended (cross) conjugation which is responsible for a bathochromic UV absorption (λ_{max} = 463 nm). In addition, the ^{13}C NMR spectra reveal long-range P–C coupling constants ($^2J_{P/C\text{-}3}$ = 13 (10) Hz, $^3J_{P/C\text{-}3a}$ = 2 (3) Hz) characteristic of iminophosphoranes.[2,9a,b] Once again, the iminophosphorane group proves to be a powerful chemical probe which facilitates the assignments of the neighboring C atom.

For the sequence **8** → **9** → **11** → **12** we assume a stepwise reaction mechanism as depicted in Scheme IV. Upon attack of the negatively polarized C-5 in **8** in a Michael-

(20) Typical bond lengths of the pyrrolo[3,4-*c*]pyridine **14b** are (in pm): N1–C2, 141.4 (4); C2–C3, 141.7 (5); C3–C4, 141.6 (4); C4–C5, 134.7 (4); C5–C6, 144.9 (5); C6–N1, 139.5 (3); C3–C9, 141.8 (4); C9–N10, 140.2 (4); N10–C11, 149.8 (5); N12–P13, 159.8 (2).

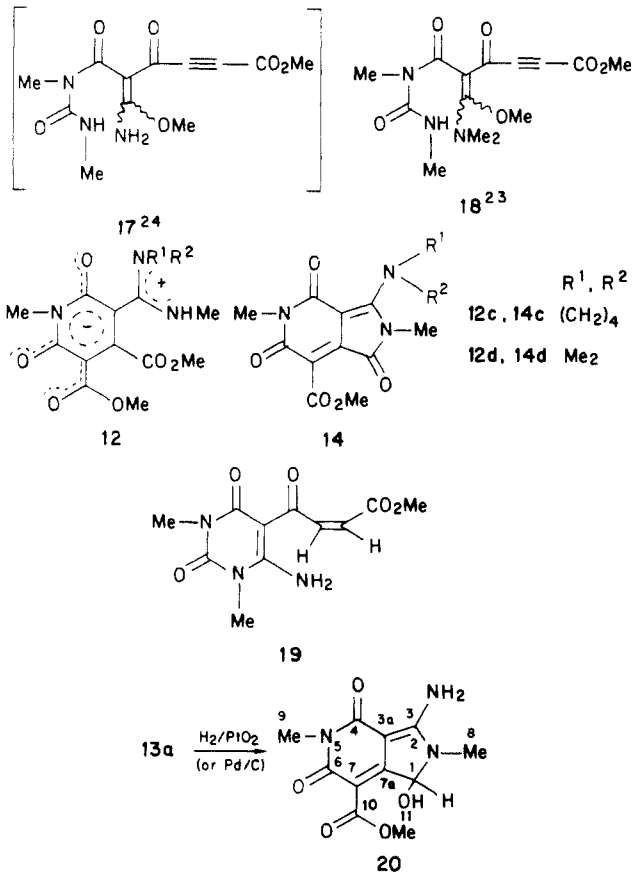
(21) (a) Ogura, H.; Saguchi, M. *Chem. Lett.* **1972**, 657; *Chem. Pharm. Bull.* **1973**, *21*, 2014; *Chem. Abstr.* **1973**, *79*, 127096. (b) In the case of barbiturate: Rao, S. A.; Mitra, R. B. *Indian J. Chem.* **1974**, *12*, 1028; *Chem. Abstr.* **1975**, *82*, 112023.

(22) Anderson, G. L.; Shim, J. L.; Broom, A. D. *J. Org. Chem.* **1973**, *42*, 993. No IR and ^{13}C NMR data are presented in this note.

(23) Kawahara, N.; Itoh, T.; Ogura, H.; Watanabe, K. A. *Chem. Pharm. Bull.* **1982**, *30*, 63; *Chem. Abstr.* **1982**, *96*, 199060.

(24) Anderson, G. L.; Broom, A. D. *J. Org. Chem.* **1977**, *42*, 4159.

Scheme V



type reaction to the triple bond in an *aprotic solvent* such as C_2Cl_4 rearrangement occurs to **11** which is stabilized by tautomerism to afford **12**. When the reaction of **8a** and acetylenic ester is carried out in ethanol, the intermediate **9** is protonated to give **10** as the main product; traces of **12** are also produced.

Hydrolysis of the iminophosphorane group of **14** in HCl gives the amines **13**. The properties of **13** (mp, NMR, IR) were identical with those reported earlier by Anderson, Shim, and Broom[25c] for a compound which was assigned the 6-amino-5-(3-carbomethoxy-2-propynoyl)-1,3-dimethyluracil structure **15** (cf. Scheme IV). This correspondence in properties prompted us to reinvestigate the synthesis of **15** for comparison with our hydrolysis product **13a**. The two samples were identical, establishing that Broom's "**15**" indeed has structure **13a**. Treatment of the product prepared according to Broom with Ph_3PCl_2 gave a product which was identical in all properties with **14**.

As a consequence, the product primarily formed from 6-amino-1,3-dimethyluracil **7a** and dimethyl acetylenedicarboxylate in Me_2SO or DMF cannot be a ring-cleaved "urea **17**".[24] It is very likely a compound closely related to the forementioned zwitterion **12a** (of course, **17** might be less stable than **12a**, being unphosphorylated).

In addition, another study has been published by Kawahara, Watanabe, et al.[23] based upon these results of Anderson and Broom[24] and discussing "new stable pyrimidine ring-opened compounds" of analogous constitution. We have resynthesized one of these "cleavage products", according to the literature,[23] namely "urea **18**" (see Scheme V). All our measurements on **18** are in good accordance with the literature data. Although **18** represents a rather unsymmetrically substituted acetylene moiety, no triple bond could be detected neither in the IR nor in the Raman spectra. The ^{13}C NMR data presented[23] (δ 93.56 and 94.34) do not unambigously indicate sp-hybridized carbon atoms (literature ^{13}C values for acetylenic esters, δ ca. 75);[26] in our opinion, these values might be exchangeable for other C atoms. With all other respects, this and the other forementioned compounds display properties so similarly that similar structures like **12c,d** and **14c** are proposed for those products.[23] The ring closure of "[2-(propioloyl)-acryloyl]urea **3b**"[23] was analogously attempted, but the data of the product obtained do not point to the formation of a 5-propioloyl-6-dimethylaminouracil; instead, we suggest formation of **14d** has occurred; the analytical data found are in good agreement with those for **13a**.

Finally, Broom et al.[25c] describe a catalytic hydrogenation of **15** which gives in their opinion the *cis*-olefin **19**. Repeating this hydrogenation both with **15** and **13a** leads to identical hydrogenation products; deuterium exchange experiments and ^{13}C NMR data reveal that instead of olefin **19** carbinol **20** has been formed by selective reduction of the pyrrole carbonyl group.

Thus, in addition to the recently reported attacks of 1,3-ambident nucleophiles such as guanidine and carbanionic reagents to the *6-position* of uracils (leading to uracil → pyrimidine, uracil → pyridine, and uracil → pyrido-[2,3-*d*]pyrimidine transformations,[27] and in addition to a novel *photochemical* ring cleavage of 1,3-dimethyluracil to an enamine,[28] the reaction type described in this communication represents a novel mode of ring-cleavage found on an uracil moiety, where the *2-carbonyl group* is attacked by a terminal carbanionic species.

Scope and limitations of this novel rearrangement, employing, e.g., azodicarboxylates are currently under investigation.

Experimental Section

Methods and Materials. Analyses were carried out by the Mikroanalytisches Laboratorium des Instituts für Organische Chemie und Biochemie, Universität Bonn. Ultraviolet spectra were obtained on a Cary-17 spectrophotometer, and infrared spectra were recorded on a Perkin-Elmer 157-G spectrophotometer. Raman spectra were taken on a Coderg LRG-800 spectrophotometer, ^1H NMR spectra on a Bruker WH-90 spectrometer, and ^{13}C NMR spectra on a Bruker WP-80 spectrometer. The mass spectrometers (MS) used were the A.E.I. (Kratos) MS-30 and MS-50. Melting points are uncorrected. The X-ray crystallographic studies were done by using an AED Syntex P-21 diffractometer at ambient temperature (see Table II).

MeCN was freshly distilled from P_2O_5, the Et_3N from KOH/absolute ethanol. All other chemicals obtained commercially were used without further purification.

1,3-Dimethyl-2,4-dioxo-6-[(triphenylphosphoranylidene)amino]pyrimidine (8). 6-Amino-1,3-dimethyluracil (**7**) (23.3 g, 150 mmol) was suspended in MeCN (500 mL). $(C_6H_5)_3P$ (41.7 g, 180 mmol) and Et_3N (30.3 g, 300 mmol) were added, and finally C_2Cl_6 (35.6 g, 150 mmol) was added. The reaction was carried out under Ar, the mixture was allowed to stir at 25 °C for 16 h, followed by filtration, and the residue was dissolved in CH_2Cl_2.

(25) (a) Broom, A. D.; Shim, J. L.; Anderson, G. L. *J. Org. Chem.* **1976**, *41*, 1095. (b) Ogura, H.; Saguchi, M. *Chem. Pharm. Bull.* **1973**, *21*, 2014; *Chem. Abstr.* **1973**, *79*, 137096. (c) Shim, J. L.; Niess, R.; Broom, A. D. *J. Org. Chem.* **1972**, *37*, 578.

(26) ^{13}C Data Bank, Vol. I, Bruker Analytische Messtechnik: Karlsruhe, 1976. In the same way, the ^{13}C NMR data (δ 88.83 and 110.23) attributed to the "5-propiolyl-6-pyrrolidinouracil **4**"[23] cannot be consistent with sp-hybridized C atoms; these values are in much better agreement with a donor-substituted alkene.

(27) (a) Hirota, K.; Watanabe, K. A.; Fox, J. J. *J. Org. Chem.* **1978**, *43*, 1193. (b) Hirota, K.; Kitade, Y.; Senda, S.; Halat, M. J.; Watanabe, K. A. *J. Am. Chem. Soc.* **1979**, *101*, 4423. (c) Hirota, K.; Kitade, Y.; Senda, S. *Heterocycles* **1980**, *14*, 407. (d) Hirota, K.; Kitade, Y.; Senda, S.; Halat, M. J.; Watanabe, K. A.; Fox, J. J. *J. Org. Chem.* **1981**, *46*, 846.

(28) Arys, M.; Christensen, T. B.; Eriksen, J. *Tetrahedron Lett.* **1984**, *25*, 1521.

Table II. Summaries of X-ray Data for 12b and 14b[a]

	12b	14b
formula	$C_{32}H_{32}N_3O_6P$	$C_{30}H_{26}N_3O_5P$
fw	585.34	539.5
space group	$P2_1/n$	$P_{\bar{1}}$
a, Å	10.064 (3)	10.673 (4)
b, Å	12.964 (5)	11.603 (3)
c, Å	22.864 (2)	11.693 (3)
α, deg		89.77 (2)
β, deg	93.85 (2)	107.10 (2)
γ, deg		108.94 (2)
V, Å^3	2978 (5)	1302.4 (7)
Z	4	2
d_{calcd}, g/cm^3	1.305	1.375
μ(Mo Kα), mm^{-1}	0.135	0.146
F(000)	1231.8	563.91
crystal size, mm	0.3 × 0.4 × 0.5	0.2 × 0.3 × 0.4
data collection instrument	AED Syntex P 21	
radiation λ, Å	Mo Kα = 0.71069 graphite, monochromated	
scan method	θ-2θ	ω
$2\theta_{max}$, deg	50.0	50.0
scan width, deg	2.0 + $\alpha_1\alpha_2$	2.0
scan speed, deg/min	2.0-20.0	
standard	1	
monitor interval	33	
no. of collected reflections	5434	4840
unobserved reflections ($I < 3\sigma$)	1347	1644
no. of unique data	3333	2928
R_{int} ($\|F\|$)	0.029	0.016
structure solution	direct methods	
refinement	block matrix, maximum 100 parameters; anisotropic temperature factors; hydrogen: "riding model"	
weighting scheme	$\omega = (\sigma^2(F) + 0.002F^2)^{-1}$; $(\sigma^2(F) + 0.0005F^2)$	
$R_{om\ unobsd}$	0.050	0.043
R_w	0.074	0.050
GOF	1.37	1.41

[a] All calculations with SHELXTL 76.

After repeated filtration the solvent was evaporated. The crude product obtained was recrystallized two times from EtOH to give white crystals (39.2 g, 63%): mp 238 °C; IR (KBr) 1680 (CO), 1635 (CO), 1575 (C=C), 1430 (N=P) cm^{-1}; UV ($CHCl_3$) λ_{max} (log ϵ) 268 (4.17), 274 (4.20) nm; ^{1}H NMR ($CDCl_3$) δ 7.53–7.89 (m, 15 H), 4.60 (d, $^4J_{PH}$ = 1.0 Hz, 1 H), 3.60 (s, 3 H), 3.25 (s, 3 H); ^{13}C NMR ($CDCl_3$, numbering cf. Scheme III) 27.36 (C-8, q), 30.27 (C-7, q), 84.52 (C-5, dd, $^3J_{PC}$ = 8.6 Hz), 127.45 (C-9, d, $^1J_{PC}$ = 103.2 Hz), 129.11 (C-11, dd, $^3J_{PC}$ = 12.8 Hz), 132.55 (C-10, dd, $^2J_{PC}$ = 9.8 Hz), 132.86 (C-12, dd, $^4J_{PC}$ = 3.6 Hz), 153.33 (C-2, d, $^4J_{PC}$ = 3.0 Hz), 157.29 (C-6, d, $^2J_{PC}$ = 11.0 Hz), 163.45 (C-4, s); MS, m/z (relative intensity) 415 (M, 100). Anal. Calcd for $C_{24}H_{22}N_3O_2P$: C, 69.39; H, 5.34; N, 10.11. Found: C, 69.57; H, 5.43; N, 9.88.

Ethyl 1,3-Dimethyl-2,4-dioxo-6-[(triphenylphosphoranylidene)amino]pyrimidine-5-carboxylate (8b). **7b**, (22.7 g, 100 mmol), 31.4 g (120 mmol) of $(C_6H_5)_3P$, and 20.2 g (200 mmol) Et_3N were suspended under Ar in 500 mL of MeCN. Then at once 23.7 g (100 mmol) of C_2Cl_6 was added in one portion to this reaction mixture, which was then allowed to stir at 25 °C for 16 h and then refluxed for 5 min. After cooling, the resulting precipitate was collected by filtration . The crude product was recrystallized two times from EtOH to afford 32.1 g (66%) of pale yellow crystals: mp 248 °C; IR (KBr) 1710 (CO), 1680 (CO), 1630 (CO), 1550 (C=C), 1440 (N=P) cm^{-1}; UV ($CHCl_3$) λ_{max} (log ϵ) 268 (4.11), 275 (4.15), 296 (4.30) nm; ^{1}H NMR ($CDCl_3$) δ 7.47–7.76 (m, 15 H), 3.44 (s, 3 H), 3.34 (s, 3 H), 3.37 (q, 2 H), 0.96 (t, 3 H); ^{13}C NMR ($CDCl_3$, cf. Scheme III) δ 13.83 (C-15, q), 27.72 (C-8, q), 31.55 (C-7, q), 59.73 (C-14, t), 92.57 (C-5, d, $^3J_{PC}$ = 2.4 Hz), 128.67 (C-11, dd, $^3J_{PC}$ = 13.4 Hz), 129.86 (C-9, d, $^1J_{PC}$ = 98.9 Hz), 132.38 (C-10, dd, $^2J_{PC}$ = 11.0 Hz), 132.80 (C-12, d), 152.28 (C-2, $^4J_{PC}$ = 2.4 Hz), 156.23 (C-6, d, $^2J_{PC}$ = 12.2 Hz), 161.46 (C-4, s), 167.57 (C-13, s); MS, m/z (relative intensity 487 (M, 35), 458 (100). Anal. Calcd for $C_{27}H_{26}N_3O_4P$: C, 66.52; H, 5.38; N, 8.62. Found: C, 66.25; H, 5.53; N, 8.26.

4,5-Dicarbomethoxy- and 4,5-Dicarbethoxy-*N*-methyl-3-[(*N*-methylamino)((*N*-triphenylphosphoranylidene)-amino)methylene]pyridine-2,6-diones (12a and 12b). To a suspension of 4.15 g (10 mmol) of **8a** in 40 mL of C_2Cl_4 was added dialkyl acetylenedicarboxylate [methyl, 2.1 g (15 mmol); ethyl, 2.55 g (15 mmol)], and the mixture was refluxed (**16a**, 8 h; **16b**, 2 h). After the reaction mixture was cooled, the crude product was collected by filtration. The product was washed three times with 20 mL of petroleum ether (bp 60–90 °C)/acetone (2:1; v:v) followed by crystallization from MeCN to give yellow-green crystals; yield **12a**, 4.4 g (79%); **12b**, 4.6 g (78.6%).

12a: mp 149 (red color change), 280 (slow approach; thermal ring closure), 248 °C (fast approach); IR (KBr) 3360 (NH), 1730, 1630 (CO), 1585, 1530 (C=C), 1405 (N=P) cm^{-1}; UV ($CHCl_3$) λ_{max} (log ϵ) 352 (4.57) nm; ^{1}H NMR (Me_2SO-d_6) δ 9.07 (dq, 1 H), 7.84–7.38 (m, 15 H), 3.45 (s, 3 H), 3.29 (s, 3 H, 2.98 (d, 3 H), 2.47 (s, 3 H); ^{13}C NMR ($CDCl_3$, cf. Scheme IV) δ 25.93 (C-7, q), 29.48 (C-11, q), 51.27 (C-16, q), 52.09 (C-17, q), 93.21 (C-5, s), 102.18 (C-3, d, $^3J_{PC}$ = 6 Hz), 125.46 (C-12, d, $^1J_{PC}$ = 105 Hz), 128.54 (C-14, dd, $^3J_{PC}$ = 13 Hz), 132.95 (C-15, d), 145.84 (C-4, s), 161.72, 161.84 (C-9,10, s), 166.57 (C-8, d, $^2J_{PC}$ = 8 Hz), 167.61, 169.15 (C-2,6, s); MS, m/z (relative intensity) (M - MeOH, 100). Anal. Calcd for $C_{30}H_{28}N_3O_6P$: C, 64.63; H, 5.06; N, 7.54. Found: C, 64.73; H, 5.17; N, 7.63.

12b: mp 169 (red color change), 280 (slow approach; thermal ring closure), 248 °C (fast approach); IR (KBr) 3370 (NH), 1730, 1670, 1630 (CO), 1590, 1530 (C=C), 1400 (N=P) cm^{-1}; UV ($CHCl_3$) λ_{max} (log ϵ) 353 (4.56) nm; ^{1}H NMR (Me_2SO-d_6) 9.11 (dq, 1 H $^4J_{PH}$ (by C-H and P-H heteronuclear decoupling) = 7 Hz), 7.87–7.38 (m, 15 H), 4.00 (q, 2 H), 3.97 (q, 2 H), 3.02 (d, 3 H), 2.53 (s, 3 H), 1.13 (t, 3 H), 0.97 (t, 3 H); ^{13}C NMR ($CDCl_3$, cf. Scheme IV) δ 13.64 (C-17, q), 14.42 (C-19, q), 25.53 (C-7, q), 29.14 (C-11, q), 58.63 (C-16, t), 60.64 (C-18, t), 93.62 (C-5, s), 100.63 (C-3, d, $^3J_{PC}$ = 6 Hz), 125.77 (C-12, d, $^1J_{PC}$ = 104 Hz), 129.14 (C-14, dd, $^3J_{PC}$ = 7 Hz), 132.97 (C-15, d), 133.75 (C-13, dd, $^2J_{PC}$ = 12 Hz), 144.38 (C-4, s), 161.16, 161.74 (C-9, 10, s), 166.17 (C-8, d, $^2J_{PC}$ = 7 Hz), 165.90, 167.75 (C-2,6,s); MS, m/z (relative intensity) 585 (M, 21), 539 (100). Anal. Calcd for $C_{32}H_{32}N_3O_6P$: C, 65.64; H, 5.51; N, 7.18. Found: C, 65.70; H, 5.49; N, 7.27.

After crystallization of **12b** from CH_2Cl_2/Et_2O yellow crystals were obtained including one molecule of CH_2Cl_2 in the crystal: mp 153 °C; IR (KBr) 3240 (NH), 1720, 1665, 1645 (CO), 1585–1540 (C=C), 1410 (N=P) cm^{-1}. Anal. Calcd for $C_{32}H_{32}N_3O_6P{\cdot}CH_2Cl_2$: C, 59.11; H, 5.11; N, 6.27. Found: C, 59.32; H, 5.18; N, 6.20.

Methyl and Ethyl 2,5-Dimethyl-3-[(triphenylphosphoranylidene)amino]-1,4,6-trioxo-1,2,5,6-tetrahydro-4*H*-pyrrolo[3,4-*c*]pyridine-7-carboxylate (14a and 14b). **12** (**12a**, 500 mg, 0.9 mmol; **12b**, 500 mg, 0.9 mmol) was heated in 10 mL of DMF for 1 h (ethyl 3 h) to 140 °C. After cooling down, **14a,b** precipitated by addition of ether. Recrystallization from ethanol afforded **14a**, 460 mg (98%), and **14b**, 370 mg (80.3%), as red-orange crystals.

14a: mp 284 °C; IR (KBr) 1750, 1680, 1625 (CO), 1570 (C=C), 1440 (N=P) cm^{-1}; UV ($CHCl_3$) λ_{max} (log ϵ) 463 (4.31), 366 (4.31) nm; ^{1}H NMR ($CDCl_3$) δ 7.82–7.40 (m, 15 H), 3.93 (s, 3 H), 3.22 (s, 3 H), 2.84 (s, 3 H); ^{13}C NMR ($CDCl_3$, cf. Scheme IV) δ 25.14 (C-13, q), 25.87 (C-8, q), 52.45 (C-15, q), 89.84 (C-3a, d, $^3J_{PC}$ = 2 Hz), 108.86 (C-7, s), 128.52 (C-9, d, $^1J_{PC}$ = 107 Hz), 128.77 (C-11, dd, J_{PC} = 10 Hz), 132.36 (C-10, dd, $^2J_{PC}$ = 10 Hz), 132.80 (C-12, d), 138.26 (C-7a, s), 158.20 (C-14, s), 163.38 (C-3, d, $^2J_{PC}$ = 13 Hz), 163.64 (C-4, s), 165.25 (C-6, s), 165.90 (C-1, d, $^4J_{PC}$ = 1 Hz); MS, m/z (relative intensity) 525 (M, 100). Anal. Calcd for $C_{29}H_{24}N_3O_5P$: C, 66.28; H, 4.60; N, 8.00. Found: C, 66.40; H, 4.42; N, 7.76.

14b: mp 283–286 °C; IR (KBr) 1740, 1680, 1625 (CO), 1560 (C=C), 1435 (N=P) cm^{-1}; UV ($CHCl_3$) λ_{max} (log ϵ) 463 (4.44), 363 (4.24) nm; ^{1}H NMR ($CDCl_3$) δ 7.80–7.38 (m, 15 H), 4.42 (q, 2 H), 3.22 (s, 3 H), 2.83 (s, 3 H), 1.38 (t, 3 H); ^{13}C NMR ($CDCl_3$, cf. Scheme IV) δ 13.86 (C-16, q), 25.08 (C-13, q), 25.78 (C-8, q), 61.40 (C-15, t), 89.87 (C-3a, d, $^3J_{PC}$ = 3 Hz), 109.37 (C-7, s), 128.64 (C-9, d, J_{PC} = 107 Hz), 128.72 (C-11, dd, $^3J_{PC}$ = 13 Hz), 132.33 (C-10, dd, J_{PC} = 10 Hz), 132.71 (C-12, d), 137.90 (C-7a, s), 158.23 (C-14, s), 163.40 (C-3, d, $^2J_{PC}$ = 10 Hz), 163.70 (C-4, s), 164.81 (C-6, s), 165.91 (C-1, d, $^4J_{PC}$ = 1 Hz); MS, m/z (relative intensity) 539 (M,

77), 467 (100). Anal. Calcd for $C_{30}H_{26}N_3O_5P$: C, 66.79; H, 4.89; N, 7.79. Found: C, 66.98; H, 4.94; N, 7.91.

Dimethyl [1,3-Dimethyl-2,4-dioxo-6-((triphenylphosphoranylidene)amino)pyrimidin-5-yl]fumarate (10a). A solution of 4.15 g (10 mmol) of **8a** in 50 mL of MeOH was refluxed, and 1.7 g (12 mmol) of dimethyl acetylenedicarboxylate in 10 mL of MeOH were added dropwise. Refluxing was continued for 30 min, and then the solvent was evaporated. The residue was dissolved in CH_2Cl_2 and crystallized at −18 °C upon addition of Et_2O: yield, 4.4 g (79%); pale-yellow crystals, mp 148 °C; IR (KBr) 1720, 1690, 1620 (CO), 1550 (C=C), 1430 (N=P) cm^{-1}; UV ($CHCl_3$) λ_{max} (log ϵ) 342 (3.99) nm; ^1H NMR ($CDCl_3$) δ 7.82–7.53 (m, 15 H), 6.06 (s, 1 H), 3.62 (s, 3 H), 3.49 (s, 3 H), 3.29 (d, 3 H), 3.10 (s, 3 H); ^{13}C NMR (Me_2SO-d_6, cf. Scheme IV) δ 27.66 (C-8, q), 32.36 (C-7, q), 51.20 (C-18, q), 51.66 (C-17, q), 97.52 (C-5, d, $^3J_{PC}$ = 5 Hz), 124.78 (C-14, d), 128.62 (C-9, d, $^1J_{PC}$ = 107 Hz), 129.45 (C-11, dd, $^3J_{PC}$ = 13 Hz), 132.37 (C-10, dd, $^2J_{PC}$ = 11 Hz), 132.87 (C-12, dd, $^4J_{PC}$ = 2 Hz), 139.85 (C-13, d), 151.43 (C-4, s), 154.77 (C-6, d, $^2J_{PC}$ = 9 Hz), 161.32 (C-2, s), 165.69 (C-15, s), 167.29 (C-15, s); MS, m/z (relative intensity) 557 (M, 52), 262 (100). Anal. Calcd for $C_{30}H_{28}N_3O_6P$: C, 65.10; H, 5.10; N, 7.60. Found: C, 64.72; H, 4.94; N, 7.60.

Diethyl [1,3-Dimethyl-2,4-dioxo-6-((triphenylphosphoranylidene)amino]pyrimidin-5-yl]fumarate (10b). A solution of 1.04 g (2.5 mmol) of **8a** and 0.57 g (3.0 mmol) of diethyl acetylenedicarboxylate in 20 mL of MeOH was stirred for 24 h at 25 °C. The solvent was evaporated at this temperature, and the yellow, resinous residue was dissolved in CH_2Cl_2 and crystallized at −18 °C upon addition of Et_2O: yield, 0.89 g (61%); yellow crystals, mp 170–172 °C; IR (KBr) 1725, 1690, 1630 (CO), 1570 (C=C), 1425 (N=P) cm^{-1}; UV ($CHCl_3$) λ_{max} (log ϵ) 348 (3.52) nm; ^1H NMR ($CDCl_3$) δ 7.73–7.40 (m, 15 H), 6.16 (s, 1 H), 4.05 (dq, 2 H), 3.98 (q, 2 H), 3.32 (d, 3 H), 3.01 (s, 3 H), 1.16 (t, 6 H); ^{13}C NMR (Me_2SO-d_6, cf. Scheme IV) δ 13.83 (C-20, q), 13.89 (C-18, q), 27.78 (C-8, q), 31.03 (C-7, q), 59.38 (C-19, t), 60.89 (C-17, t), 97.30 (C-5, d, $^3J_{PC}$ = 6 Hz), 128.66 (C-11, dd, $^3J_{PC}$ = 13 Hz), 129.40 (C-9, d, $^1J_{PC}$ = 105 Hz), 130.07 (C-14, d), 132.39 (C-12, dd, J_{PC} = 3 Hz), 132.48 (C-10, dd, $^2J_{PC}$ = 10 Hz), 139.31 (C-13, d), 152.65 (C-4, s), 153.72 (C-6, d, $^2J_{PC}$ = 5 Hz), 161.43 (C-2, d, $^4J_{PC}$ = 2 Hz), 164.94 (C-15, s), 166.42 (C-15, d); MS, m/z (relative intensity) 585 (M, 80), 262 (100). Anal. Calcd for $C_{32}H_{32}N_3O_6P$: C, 65.64; H, 5.51; N, 7.18. Found: C, 65.96; H, 5.40; N, 7.13.

Methyl and Ethyl 3-Amino-2,5-dimethyl-1,4,6-trioxo-1,2,5,6-tetrahydro-4*H*-pyrrolo[3,4-*c*]pyridine-7-carboxylate (13a and 13b). To an alcoholic solution of **14** (**14a**, 2.6 g (5 mmol) in 10 mL of MeOH; **14b**, 0.56 g (1 mmol) in 30 mL of EtOH) was added aqueous HCl (**14a**, 10 mL of 0.74; aqueous HCl; **14b**, 1 mL of 37% aqueous HCl). Then the reaction mixture was refluxed for 6 h. Crystallization at −18 °C gave the crude product, which was purified by recrystallization from MeOH (**13a**) or EtOH (**13b**) to give red crystals: yield **13a**, 0.5 g (38%); **13b**, 0.12 g (43%).

13a: mp 302 °C (lit.[25c] mp 300–301 °C); IR (KBr) 3350 (NH_2), 1760, 1730, 1670, (CO), 1580 (C=C) cm^{-1}; UV (H_2O) λ_{max} (log ϵ) [pH 1] 437 (3.87), 332 (3.81), 268 (4.23), [pH 7] 436 (3.89), 327 (3.37), 268 (4.23) nm; ^1H NMR (Me_2SO-d_6) δ 9.87 (s, 1 H), 9.35 (s, 1 H), 3.75 (s, 3 H), 3.16 (s, 3 H), 3.10 (s, 3 H) [lit.[22] ^1H NMR (Me_2SO-d_6) δ 9.97 (s, 1 H), 9.37 (s, 1 H), 3.77 (s, 3 H), 3.17 (s, 3 H), 3.13 (s, 3 H)]; ^{13}C NMR (Me_2SO-d_6, cf. Scheme IV) δ 25.77, 25.86 (C-8,9, q), 52.14 (C-11, q), 85.77 (C-3a, s), 107.46 (C-7, s), 136.25 (C-7a, s), 158.77 (C-1, s), 160.89 (C-3, s), 163.17 (C-10, s), 164.56 (C-6, s) 165.23 (C-4, s); MS, m/z (relative intensity) 265 (M, 77), 234 (100). Anal. Calcd for $C_{11}H_{11}N_3O_5$: C, 49.81; H, 4.18; N, 15.84. Found: C, 49.91; H, 4.29; N, 15.53.

13b: mp 337 °C; IR (KBr) 3360 (NH_2), 1760, 1730, 1665 (CO), 1575 (C=C) cm^{-1}; UV (H_2O) λ_{max} (log ϵ) [pH 7] 438 (3.31), 327 (2.94), 275 (3.56) nm; ^1H NMR (Me_2SO-d_6) δ 9.84 (s, 1 H), 9.36 (s, 1 H), 4.22 (q, 2 H), 3.16 (s, 3 H), 3.09 (s, 3 H), 1.24 (t, 3 H); ^{13}C NMR (Me_2SO-d_6, cf. Scheme IV) δ 13.94 (C-12, q), 25.71, 25.77 (C-8,9, q), 60.85 (C-11, t), 85.52 (C-3a, s), 107.97 (C-7, s), 135.86 (C-7a, s), 158.74 (C-1, s), 160.83 (C-3, s), 163.17 (C-10, s), 163.99 (C-6, s), 165.17 (C-4, s); MS, m/z (relative intensity), 279 (M, 77), 207 (100). Anal. Calcd for $C_{12}H_{13}N_3O_5$: C, 51.61; H, 4.69; N, 15.05. Found: C, 51.28; H, 4.33; N, 15.26.

"5-Propynoyluracil 3a" of Broom et al.[25c] (15). According to the procedure given in lit.,[25c] 1.35 g (51%) of **15** was obtained: mp 302 °C (lit.[25c] mp 300–301 °C); **13a**, mp 302 °C; **13a**/**15**, mixed mp 301 °C. **15** proves to be identical with **13a** in every respect. As we have found, the use of MeCN as solvent is advantageous.

Phosphorylation of 15[25c] [To Give Methyl 2,5-Dimethyl-3-[(triphenylphosphoranylidene)amino]-1,4,6-trioxo-1,2,5,6-tetrahydro-4*H*-pyrrolo[3,4-*c*]pyridine-7-carboxylate (14a)]. To a suspension of 0.65 g (2.5 mmol) of **15** (made according to the literature[25c]) were added 0.79 g (3 mmol) of $(C_6H_5)_3P$ and 0.5 g (5 mmol) of NEt_3 in 50 mL MeCN 0.59 g (2.5 mmol) of C_2Cl_6, the reaction mixture being kept under Ar. Then the mixture was stirred at 25 °C for 8 h, and the product was filtered off. Recrystallization from EtOH gave 0.85 g (65%) of red-orange crystals. The compound **16** obtained, proved to be identical with **14a** in every respect.

"2-[(3-Methoxycarbonyl)propioloyl]acryloylurea 3b" of Kawahara, Watanabe, et al.[23] (18). According to the procedure given in the literature[23] 110 mg (39%) of **18** was obtained: mp 239 °C (lit.[23] mp 240 °C). IR and Laser Raman spectra have been measured, but no C≡C band was detectable.

Analogous Cyclocondensation of "2-Propioloylacryloylurea 3b"[23] to "5-Propiolyl-6-(dimethylamino)uracil"—Our Proposal, 14d. "2-(Propioloyl)acryloylurea" (100 mg, 0.31 mmol; (i.e., **3b** of Kawahara, Watanabe, et al.[23]) was refluxed in MeCN for 6 h; after evaporation of the solvent, the residue was dissolved in CH_2Cl_2 and the product precipitated by addition of ether: yield, 35 mg (38.5%); mp 194 °C; UV (DMF) λ_{max} (log ϵ) 447 (4.00), 283 (4.35) nm; IR (KBr) 1760, 1720, 1685 (CO), 1620 (C=C) cm^{-1} (no C≡C band); ^1H NMR (Me_2SO-d_6) δ 3.76 (s, 3 H, OMe), 3.32, 3.30, 3.26, 3.14 (all s, 3 H, NMe); MS, m/z (relative intensity) 293 (M^+, 100); high-resolution MS for $C_{13}H_{15}N_3O_5$, found 293.1013, calcd 293.1008. Anal. Calcd for $C_{13}H_{15}N_3O_5$: C, 53.24; H, 5.16; N, 14.33. Found: C, 53.04; H, 5.34; N, 14.28.

Methyl 3-Amino-1,2,5,6-tetrahydro-1-hydroxy-2,5-dimethyl-4,6-dioxo-4*H*-pyrrolo[3,4-*c*]pyridine-7-carboxylate (20). Procedure A. **13a** (500 mg, 1.9 mmol) was dissolved in dimethoxyethane–water (1:1) and hydrogenated at 100 °C and 72.5 psi (5 bar) with 250 mg of PtO_2 as catalyst for 24 h. After filtration through silica gel the filtrate was evaported. Titration with MeOH gave 86 mg of **20** (17%).

Procedure B. **13a** (500 mg, 1.9 mmol) was dissolved in 60 mL of MeOH (under argon) and hydrogenated 24 h at 80 °C and 72.5 psi (5 bar) with 500 mg of 5% Pd/C as catalyst. Workup like procedure A and recrystallization from MeOH gave 360 mg (71%) of **20**.

20: mp 309 °C (lit.[25c] mp 310 °C dec); IR (KBr) 3360, 3230 sh (NH_2), 3050 br (OH), 1720, 1665 (CO), 1630, 1590 (C=C), 1520 (δ_{NH_2}, C–O) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 8.68, 8.07 (2 s, NH_2, exchangeable), 6.93 (d, OH, exchangeable, J = 7 Hz), 5.92 (d, CH, J = 7 Hz), 3.61 (s, OMe), 3.09 (s, NMe), 3.01 (s, NMe); [lit.[25c] ^1H NMR (cf. formula **19**) δ 8.48, 7.87 (2 s, NH_2), 6.77, 5.80 (2 d, 2 =CH, J = 9 Hz), 3.58 (s, OMe), 3.05 (s, NMe), 2.97 (s, NMe)]; ^{13}C NMR (Me_2SO-d_6) δ 25.48 (q, C-9), 27.72 (q, C-8), 50.60 (q, C-11), 87.14 (d, C-1), 91.90 (s, C-3a), 97.76 (s, C-7a), 158.58 (s, C-7), 160.13 (s, C-3), 160.23 (s, C-4), 162.56 (s, C-6), 165.09 (s, C-10); MS, m/z (relative intensity) 267 (M^+, 100); high-resolution MS for $C_{11}H_{13}N_3O_5$, found 267.0856, calcd 267.08520.

Crystallographic Data. For details of these X-ray investigations, cf. Fachinformationszentrum Energie, Physik, Mathematik, D-7514 Eggenstein-Leopoldshafen 2, FRG, referring to the code No. CSD 51244, the author's name, and the citation of this work.

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