Reactions of Uracils, 16[1]

Substituted 6-Vinyl-2,4(1*H*,3*H*)-pyrimidinediones in Cycloaddition and Michael-Type Reactions: Pyrido[2,3-*d*]pyrimidines, Pyrrolo[3,4-*c*]pyridines, and Quinazolines

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Electron-rich 6-vinyl- and 6-(azavinyl)pyrimidinediones, such as 6-{[(dimethylamino)methylene]amino}- (**1**) and 6-[2-(dimethylamino)vinyl]-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinediones (**8**), undergo cycloaddition reactions with electron deficient olefins to give pyrido[2,3-*d*]pyrimidines (**3a–e**) and quinazolines (**9a–c**), respectively, after elimination of dimethylamine from the 1:1 cycloadducts and oxidative aromatization. With dimethyl acetylenedicarboxylate, pyrrolo[3,4-*c*]pyridines **5**, **11**, and **15** were obtained due to an initial Michael addition and subsequent ring transformation reaction. Stable Michael adducts were also obtained from reactions of **1** with azodicarboxylates. The stable adducts **6a–c** were thermally converted into 8-(dimethylamino)theophylline (**7**).

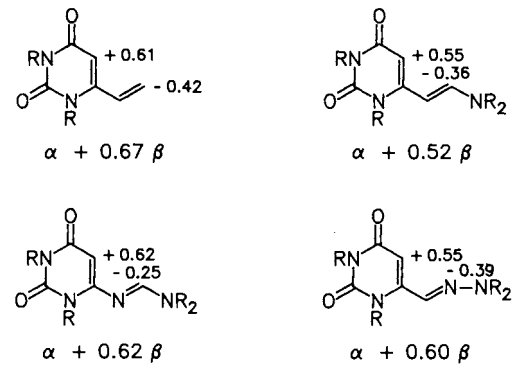
Reaktionen von Uracilen, 16[1]. – Substituierte 6-Vinyl-2,4(1*H*,3*H*)-pyrimidindione in Cycloadditions- und Michael-Additions-Reaktionen: Pyrido[2,3-*d*]pyrimidine, Pyrrolo[3,4-*c*]pyridine und Chinazoline

Elektronenreiche 6-Vinyl- und 6-(Azavinyl)pyrimidindione, wie z.B. 6-{[(Dimethylamino)methylen]amino}- (**1**) und 6-[2-(Dimethylamino)vinyl]-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidindion (**8**), reagieren mit elektronenarmen Olefinen unter Cycloaddition. Nach Eliminierung von Dimethylamin und oxidativer Aromatisierung ergeben die 1:1-Cycloaddukte **2a–e** die Pyrido[2,3-*d*]-pyrimidine **3a–e** bzw. die Chinazoline **9a–c**. Mit Acetylendicarbonsäure-dimethylester entstehen durch Michael-Addition und anschließende Umlagerung die Pyrrolo[3,4-*c*]pyridine **5**, **11** und **15**. Die stabilen Michael-Addukte **6a–c** werden durch Einwirkung von Azodicarbonsäureester auf **1** erhalten; sie lassen sich thermisch in 8-(Dimethylamino)theophyllin (**7**) umwandeln.

Quinazolines and pyrido[2,3-*d*]pyrimidines represent a broad class of compounds which have received considerable attention over the past years due to their wide range of biological activities[2a,b]. As such, these fused heterocycles have been extensively investigated, and their synthetic preparations are well documented[2a,c]. Most of these preparations rely on cyclocondensation reactions from pyrimidine or pyridine intermediates. However, this type of stepwise synthetic strategy limits the synthetic flexibility. We now describe a new synthetic route to these heterocycles based on [4 + 2] cycloaddition reactions, which allow access to a range of structural variations by modification of the reacting components.

In the past a cycloaddition approach has had little appeal since the dienophilic nature of the pyrimidine ring is rather limited, and the diene properties of vinylpyrimidines had not yet been established[3]. It was postulated that if a vinylpyrimidine system were appropriately substituted with strong electron donating groups, cycloaddition might occur with electron deficient dienophiles. Recent work in which the diene character of furan was enhanced by incorporation of a dimethylhydrazono group[4] as well as the abilities of methacrolein dimethylhydrazone[5] and 1-(dimethylamino)-3-methyl-2-azabutadiene[6] to function as azadienes suggests that the dienic character of vinylpyrimidines would be increased by similar substituents. This is further supported by HOMO calculations[7] which show an increase in the HOMO energies of the 6-aminovinyl-, 6-aminomethyleneamino-, and 6-hydrazonomethyl derivatives of 2,4-pyrimidinedione relative to 6-vinyl-2,4-pyrimidinedione (see Scheme 1).

Scheme 1. Energies and coefficients of the HOMO of uracil model compounds



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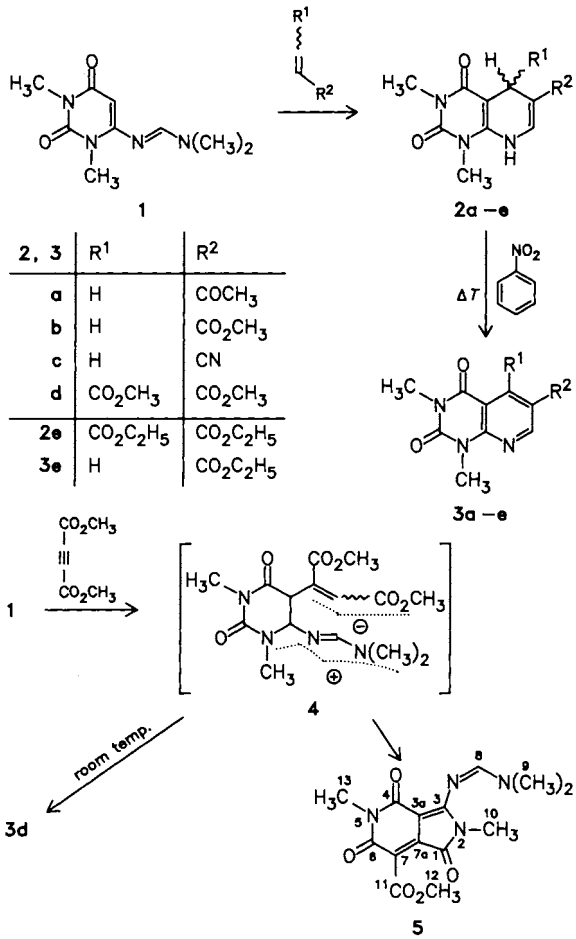
Reactions of 6-{[(Dimethylamino)methylene]amino}-1,3-dimethyluracil (1)

Uracil **1**, readily prepared from 6-amino-1,3-dimethyluracil and dimethylformamide dimethyl acetal, reacted with methyl vinyl ketone in toluene (110°C, 8 h) to give, after elimination of dimethylamine and tautomerization, the 6-acetyl-5,8-dihydropyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione **2a** as the sole product. Spectral data were consistent with the assigned structure, especially ν_{NH} 3400 to 3200 cm^{-1}.

Cycloaddition of **1** to methyl acrylate and acrylonitrile also resulted in the formation of the 5,8-dihydropyrido[2,3-*d*]pyrimidinediones **2b** and **2c** regioselectively. The high regioselectivity observed in these reactions is consistent with the electron-donating effect of the dimethylamino substituent, which increases the nucleophilicity of the C-5 position[6-8], and with the established reactivities of the olefins.

The dihydro adducts **2a–c** were converted into their aromatic analogues **3a–c** in high yields by oxidative aromatization in refluxing nitrobenzene[9].



2, 3	R^1	R^2
a	H	$COCH_3$
b	H	CO_2CH_3
c	H	CN
d	CO_2CH_3	CO_2CH_3
2e	$CO_2C_2H_5$	$CO_2C_2H_5$
3e	H	$CO_2C_2H_5$

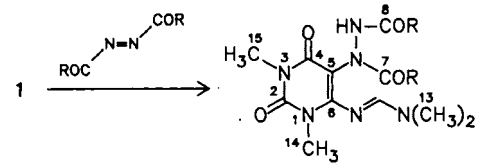
Reaction of **1** with disubstituted olefins also afforded cycloaddition products. Thus, treatment of **1** with both dimethyl fumarate and diethyl maleate gave, after column chromatography (silica gel, ethyl acetate), **2e** in 65% yield. No attempt was made to resolve these adducts. However, while **2d** afforded **3d** upon refluxing in nitrobenzene, similar treatment of **2e** resulted in the thermal elimination of ethyl formate from the cycloadduct yielding the ethyl pyrido[2,3-*d*]pyrimidine-6-carboxylate **3e**. The compound was characterized by its ^{1}H-NMR spectrum, which showed *meta* coupling between 5-H and 7-H on the order of 2.1 Hz. No 5-ethoxycarbonyl derivative was detected in the reaction mixture.

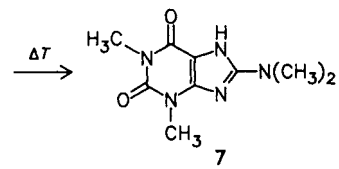
In contrast, reaction of **1** with fumaronitrile (acetonitrile, 82°C, 12 h) afforded **3c** directly by elimination of HCN in addition to dimethylamine from the 1:1 cycloadduct. As in the previous reaction only the 6-substituted derivative was obtained.

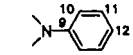
Cycloaddition of **1** with dimethyl acetylenedicarboxylate (DMAD) has the potential of leading directly to the aromatized pyrido[2,3-*d*]pyrimidine **3d**. However, the reaction of **1** with DMAD in acetonitrile (room temp., 36 h) gave a mixture of **3d** and pyrrolo[3,4-*c*]pyridine **5** in a 1:2 ratio. The formation of **5** is in accordance with the reported heterocyclic transformation reactions of 6-aminouracils and acetylenedicarboxylates which lead to zwitterionic amidinium pyridinedionates and pyrrolo[3,4-*c*]pyridines[10]. The isolation of both **3d** and **5** in this reaction also suggests a common intermediate whereby the terminal carbanion arising from the initial Michael adduct **4** either attacks the imino carbon atom eliminating dimethylamine to give **3d**, or attacks competitively the 2-C=O of the uracil moiety and, with subsequent transformation and elimination of MeOH, affords **5**.

When the reaction was carried out in boiling toluene (16 h) or chloroform (18 h), **5** was obtained exclusively in 70% yield. The structure of **5** was established unambiguously by single-crystal X-ray analysis[11].

The observation that **1** forms an initial Michael adduct with DMAD and the well documented ability of 6-amino- and 6-(alkylamino)uracils to undergo Michael additions with azodicarboxylates[12] prompted us to examine analogous reactions of **1**.





6	R	R
a	R–R:	
b	$O-CH_2-CH_3$	$O-CH_2CH_3$
c	$O-C_6H_5$	$O-C_6H_5$

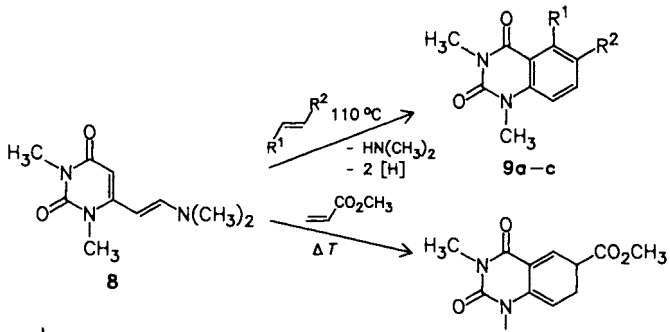
Treatment of **1** with 4-phenyl-1,2,4-triazoline-3,5-dione (4-Ph-TAD)[13] in acetonitrile (room temp., 1 h) gave the 5-hydrazinoprimidine **6a**, which separated directly from the reaction mixture and was characterized by ν_{NH} 2890 and $\nu_{C=O}$ 1770, 1710, and 1660 cm^{-1}. A similar reaction of **1** with diethyl or diphenyl azodicarboxylate in toluene (110°C,

8 h) gave the 5-hydrazinopyrimidines **6b,c** in 60 and 35% yields, respectively.

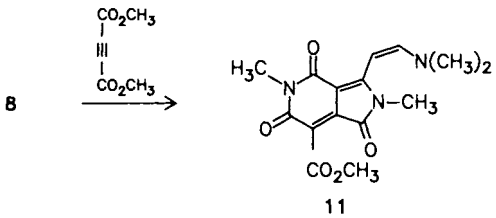
These Michael adducts are key intermediates in the formation of theophylline derivatives by thermal cyclization reactions[14]. Thus, heating **6b** or **6c** above 230°C or in refluxing nitrobenzene resulted in the formation of 8-(dimethylamino)theophylline (**7**)[14,15]. Similar treatment of **6a** also gave **7**, but in low yield, as indicated by TLC and high-resolution mass spectrometry. In this instance, **7** could not be isolated in pure form.

Reactions of 6-[2-(Dimethylamino)vinyl]-1,3-dimethyluracil (8)

In contrast to the reactions of **1**, uracil **8**[16] reacted with electron deficient olefins to give the aromatic 5,6-disubstituted quinazoline-2,4-diones **9a–c** directly, albeit in reduced yields. The reactions proceed by formation of a 1:1 cycloadduct, 1,4-elimination of dimethylamine, and oxidative aromatization. Thus, reaction of **8** with methyl vinyl ketone in toluene (110°C, 16 h) gave **9a** exclusively, as indicated by a 1.4 Hz coupling between 5-H and 7-H. The regioselectivity of the reaction is in accordance with the increased nucleophilicity of C-5 compared to C-2′ as shown by the HOMO coefficients[7] and the established reactivity of the dienophile.



9	R^1	R^2
a	H	$COCH_3$
b	CO_2CH_3	CO_2CH_3
c	$CO_2C_2H_5$	$CO_2C_2H_5$

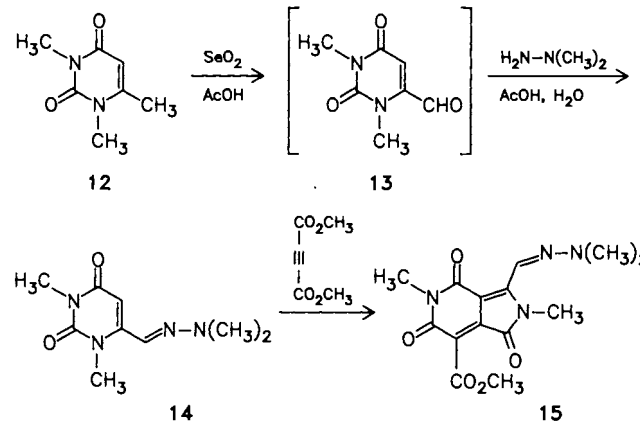


Similar reaction of **8** with dimethyl and diethyl fumarate and diethyl maleate also gave the quinazolines **9b** and **9c** as the sole products. With methyl acrylate aromatization of the cycloadduct did not occur, and the 6,7-dihydropyrimidine **10** was obtained as a result of elimination of dimethylamine followed by isomerization.

Reaction of **8** with DMAD in boiling toluene (6 h) afforded the pyrrolo[3,4-*c*]pyridine **11** in 49% yield in a manner analogous to the reaction of **1** with DMAD. Attempts to obtain the 5,6-disubstituted quinazoline **9b** by performing the reaction under less vigorous conditions and for longer reaction times were unsuccessful. In addition, **8** was found to be unreactive towards azodicarboxylates.

Reactions of 1,3-Dimethyluracil-6-carbaldehyde Dimethylhydrazone (14)

Hydrazone **14** was obtained by selenium dioxide oxidation of 1,3,6-trimethyluracil (**12**) to the aldehyde **13**[17] and subsequent condensation with *N,N*-dimethylhydrazine.



Treatment of **14** with DMAD in toluene (110°C, 8 h) afforded the pyrrolo[3,4-*c*]pyridine **15** in low yield. Further reactions of **14** with other dienophiles under a variety of conditions have, to this point, resulted in no isolable products. This may be due to the instability of **14**, which decomposes even on storage or in the presence of silica gel.

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Experimental

IR spectra: Perkin-Elmer 157-G. – ^{1}H NMR spectra: Bruker WH-90 and AC-200, TMS as int. standard. – ^{13}C-NMR spectra: Bruker WH-90 and AC-200, $CDCl_3$, 77.10 ppm, int. standard. – MS: MS-30 and MS-50 of Kratos (A.E.I.). – Melting points: not corrected. – Elemental analyses: Analytical Department of our Institute and Mikroanalytisches Laboratorium Pascher, D-5480 Remagen.

6-{[(Dimethylamino)methylene]amino}-1,3-dimethyluracil (**1**): 10.0 g (64 mmol) of 6-amino-1,3-dimethyluracil and 7.7 g (64 mmol) of dimethylformamide dimethyl acetal were heated under reflux in 80 ml of anhydrous benzene for 6 h during which the starting material slowly went into solution. The reaction mixture was cooled and filtered affording small amounts of starting amine. Evaporation of the benzene solution and recrystallization of the residue from dichloromethane/hexane afforded the product as fluffy pale yellow needles; yield 9.0 g (66%); m.p. 148–150°C. – IR (KBr): $\tilde{\nu}$ = 1700, 1630 (CO), 1630 cm^{-1} (C=N). – ^{1}H NMR ($CDCl_3$): δ = 7.67 (d, 1H, CH, J = 0.4 Hz), 5.02 (s, 1H, 5-H), 3.35 (s, 3H, NCH_3), 3.27

(d, 3H, NCH_3), 3.08 (s, 3H, $H_3C-N-CH_3$), 3.02 (s, 3H, $H_3C-N-CH_3$, J = 0.4 Hz). – MS: m/z (%) = 210 (M^+, 85).

$C_9H_{14}N_4O_2$ (210.2) Calcd. C 51.41 H 6.71 N 26.65
Found C 51.29 H 6.65 N 26.87

Methyl 3-{[(Dimethylamino)methylene]amino}-2,4,5,6-tetrahydro-2,5-dimethyl-1,4,6-trioxo-1H-pyrrolo[3,4-c]pyridine-7-carboxylate (**5**): 1.0 g (4.8 mmol) of uracil **1** and 0.70 g (4.9 mmol) of dimethyl acetylenedicarboxylate (DMAD) in 30 ml of anhydrous toluene were heated under reflux for 6 h. The solution became dark red after 2 h. Toluene was removed under reduced pressure and the residue subjected to column chromatography (silica gel, ethyl acetate). Bright red microneedles were isolated, yield 1.1 g (72%); m.p. 301–302°C. – IR (KBr): $\tilde{\nu}$ = 1750, 1730, 1615 cm^{-1} (CO). – ^1H NMR ($CDCl_3$): δ = 10.11 (dd, 1H, N=CH, J = 0.71, 0.93 Hz), 3.91 (s, 3H, CO_2CH_3), 3.42 (d, 3H, $H_3C-N-CH_3$, J = 0.71 Hz), 3.30 (d, $H_3C-N-CH_3$, J = 0.93 Hz), 3.28 (s, 3H, NCH_3), 3.12 (s, 3H, NCH_3). – ^{13}C NMR ($CDCl_3$): δ = 166.95, 165.34, 164.72, 163.46 (C-1,4,6,11, exchangeable), 164.30 (C-8), 159.99 (C-3), 137.66 (C-7a), 111.80 (C-7), 89.72 (C-3a), 52.76 (C-12), 42.79, 35.77 (C-9, *E,Z* isomers), 26.86 (C-10), 25.73 (C-13). – MS: m/z (%) = 321 (M^+, 100).

$C_{14}H_{16}N_4O_5$ (320.3) Calcd. C 52.49 H 5.04 N 17.49
Found C 52.30 H 5.00 N 17.22

Dimethyl 1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrido[2,3-d]pyrimidine-5,6-dicarboxylate (**3d**) *and* **5**: 1.0 g (4.8 mmol) of uracil **1** and 0.70 g (4.9 mmol) of DMAD were stirred in 20 ml of anhydrous acetonitrile at room temp. for 36 h. The solvent was removed under reduced pressure affording a dark oil which was triturated with diethyl ether/ethanol (1:1) yielding a light tan solid. Chromatography, eluting with ethyl acetate, gave **3d** as colorless prisms; yield 0.14 g (9.6%). From the ether filtrate a precipitate formed after cooling for ca. 12 h. Recrystallization from ethyl acetate gave **5**, identical with that obtained by the previous method; yield 0.3 g (20%).

3d: m.p. 159–160°C (ethyl acetate/hexane). – IR (KBr): $\tilde{\nu}$ = 1750, 1725, 1670 cm^{-1} (CO). – ^1H NMR ($CDCl_3$): δ = 9.24 (s, 1H, 7-H), 4.05 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 3.69 (s, 3H, N-CH_3), 3.40 (s, 3H, N-CH_3). – MS: m/z (%) = 307 (M^+, 55).

$C_{13}H_{13}N_3O_6$ (307.3) Calcd. C 50.81 H 4.26 N 16.68
Found C 50.72 H 4.22 N 13.67

Cycloadducts of **1** *with Olefinic Dienophils*

a) *Isolation of the Dihydro Adducts* **2a–e**

6-Acetyl-5,8-dihydro-1,3-dimethylpyrido[2,3-d]pyrimidine-2,4(1-H,3H)-dione (**2a**): 1.0 g (4.8 mmol) of uracil **1** and 0.44 ml (5.0 mmol) of methyl vinyl ketone were heated to reflux in 30 ml of toluene for 8 h. The reaction mixture was cooled and the solid which separated filtered. Crystallization from chloroform/ethanol gave colorless plates; yield 0.70 g (62%), m.p. 237–238°C. – IR (KBr): $\tilde{\nu}$ = 3400–3200 (NH), 1710, 1680, 1660 cm^{-1} (CO). – ^1H NMR ([D_6]DMSO): δ = 9.27 (br., s, 1H, NH), 7.20 (s, 1H, 7-H), 3.32 (br. overlapping, 4H, NCH_3 and HC*H*), 3.19 (s, 3H, $COCH_3$), 3.15 (s, 3H, NCH_3), 3.07 (s, 1H, HC*H*). – MS: m/z (%) = 235 (M^+, 100).

$C_{11}H_{13}N_3O_3$ (235.2) Calcd. C 56.15 H 5.57 N 17.86
Found C 56.14 H 5.47 H 17.97

The following compounds were obtained by the preceding procedure:

Methyl 1,2,3,4,5,8-Hexahydro-1,3-dimethyl-2,4-dioxopyrido[2,3-d]pyrimidine-6-carboxylate (**2b**): Colorless prisms (chloroform/ethanol), 0.65 g (54%), m.p. 258–260°C. – IR (KBr): $\tilde{\nu}$ = 3480–3250 (NH), 1710, 1620 cm^{-1} (CO). – ^1H NMR ([D_6]DMSO and $CDCl_3$): δ = 8.83 (br. d, 1H, NH, J = 5 Hz), 6.94 (d, 1H, 7-H, J = 5 Hz), 3.58 (s, 3H, OCH_3), 3.23 (s, 3H, NCH_3), 3.12 and 3.06 (2 × s, 2H, CH_2), 3.11 (s, 3H, NCH_3). – MS: m/z (%) = 251 (M^+, 60).

$C_{11}H_{13}N_3O_4$ (251.2) Calcd. C 52.58 H 5.22 N 16.73
Found C 52.40 H 5.21 N 16.53

1,2,3,4,5,8-Hexahydro-1,3-dimethyl-2,4-dioxopyrido[2,3-d]pyrimidine-6-carbonitrile (**2c**): Colorless amorphous solid (ethyl acetate); yield 0.35 g (33%), m.p. 236–237°C. – IR (KBr): $\tilde{\nu}$ = 3480–3250 (NH), 2225 (C≡N), 1700, 1630 cm^{-1} (CO). – ^1H NMR ([D_6]-DMSO): δ = 9.42 (br. s, 1H, NH), 7.03 (br. s, 1H, 7-H), 3.35 and 3.18 (2 × s, 2H, CH_2), 3.27 (s, 3H, NCH_3), 3.12 (s, 3H, NCH_3). – MS: m/z (%) = 218 (M^+, 78).

$C_{10}H_{10}N_4O_2$ (218.2) Calcd. C 55.04 H 4.62 N 25.68
Found C 55.20 H 4.80 N 25.51

Dimethyl 1,2,3,4,5,8-Hexahydro-1,3-dimethyl-2,4-dioxopyrido[2,3-d]pyrimidine-5,6-dicarboxylate (**2d**): Colorless amorphous solid (ethyl acetate), 0.81 g (55%), m.p. 236–238°C. – IR (KBr): $\tilde{\nu}$ = 3320–3180 (NH), 1780, 1720, 1615 cm^{-1} (CO). – ^1H NMR ([D_6]DMSO and $CDCl_3$): δ = 9.45 (br. d, 1H, NH, J = 6 Hz), 7.22 (d, 1H, 7-H, J = 6 Hz), 4.61 (s, 1H, 5-H), 3.65 (s, 3H, OCH_3), 3.57 (s, 3H, OCH_3), 3.34 (s, 3H, NCH_3), 3.19 (s, 3H, NCH_3). – MS: m/z (%) = 307 (M^+ – 2, 9), 325 (M^+ – 2 + H_2O, 8).

$C_{13}H_{15}N_3O_6$ (309.3) Calcd. C 50.48 H 4.89 N 13.89
Found C 50.52 H 5.09 N 13.48

Diethyl 1,2,3,4,5,8-Hexahydro-1,3-dimethyl-2,4-dioxopyrido[2,3-d]pyrimidine-5,6-dicarboxylate (**2e**): Colorless amorphous solid, purified by column chromatography (silica gel), eluting with ethyl acetate; yield 1.05 g (65%), m.p. 211–212°C (ethyl acetate). – IR (KBr): $\tilde{\nu}$ = 3470–3200 (NH), 1730, 1700, 1630 cm^{-1} (CO). – ^1H NMR ($CDCl_3$). δ = 8.26 (br. d, 1H, NH, J = 3.6 Hz), 7.33 (d, 1H, 7-H, J = 3.6 Hz), 4.74 (s, 1H, 5-H), 4.20 (overlapping q, 4H, 2 × CH_2CH_3, J = 8.5 Hz), 3.33 (s, 1H, NCH_3), 3.30 (s, 3H, NCH_3), 1.23 (overlapping t, 6H, 2 × CH_2CH_3, J = 8.5 Hz). – MS: m/z (%) = 337 (M^+, 6).

$C_{15}H_{19}N_3O_6$ (337.3) Calcd. C 53.40 H 5.68 N 12.46
Found C 53.10 H 5.75 N 12.39

b) *Oxidative Aromatization of the Dihydroadducts* **2a–e**

6-Acetyl-1,3-dimethylpyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (**3a**): 100 mg (0.40 mmol) of **2a** was refluxed in 5 ml of nitrobenzene for 3 h. The reaction mixture cooled to room temp., and petroleum ether (60–68°C) was added till a precipitate formed with vigorous scratching. After cooling to +10°C the separated product was collected. Recrystallization from diethyl ether gave light tan prisms, yield 80 mg (81%), m.p. 162–163°C. – IR (KBr): $\tilde{\nu}$ = 1720, 1670 (CO), 1600 cm^{-1} (C=N). – ^1H NMR ($CDCl_3$): δ = 9.20 (d, 1H, 7-H, $J_{5,7}$ = 2.1 Hz), 8.87 (d, 1H, 5-H, $J_{5,7}$ = 2.1 Hz), 3.69 (s, 3H, NCH_3), 3.44 (s, 3H, NCH_3), 2.58 (s, 3H, OCH_3). – MS: m/z (%) = 233 (M^+, 43).

$C_{11}H_{11}N_3O_3$ (233.2)
Calcd. (× 1/6 H_2O) C 55.92 H 4.83 N 17.78
Found C 56.23 H 5.16 N 17.95

The following compounds were obtained by this procedure:

Methyl 1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrido[2,3-d]pyrimidine-6-carboxylate (**3b**): Colorless needles, yield 72 mg (73%), m.p. 126–127°C. – IR (KBr): $\tilde{\nu}$ = 1740, 1720, 1680 (CO), 1605 cm^{-1} (C=N). – ^1H NMR ($CDCl_3$): δ = 9.20 (d, 1H, 7-H, $J_{5,7}$ = 2 Hz), 8.98 (d, 1H, 5-H, $J_{5,7}$ = 2 Hz), 3.90 (s, 3H, NCH_3),

3.68 (s, 3H, NCH_3), 3.43 (s, 3H, OCH_3). – MS: *m/z* (%) = 249 (M^+, 100).

$C_{11}H_{11}N_3O_4$ (249.2) Calcd. C 53.00 H 4.45 N 16.86
Found C 53.03 H 4.48 N 16.84

1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrido[2,3-d]pyrimidine-6-carbonitrile (**3c**): Colorless needles (ethyl acetate/hexane), yield 61 mg (70%), m.p. 182–183°C. – IR (KBr): $\tilde{\nu}$ = 2240 (C≡N), 1720, 1660 (CO), 1610 cm^{-1} (C=N). – ^1H NMR ($CDCl_3$): δ = 8.89 (d, 1H, 7-H, $J_{5,7}$ = 2.1 Hz), 8.72 (d, 1H, 5-H, $J_{5,7}$ = 2.1 Hz), 3.70 (s, 3H, NCH_3), 3.47 (s, 3H, NCH_3). – MS: *m/z* (%) = 216 (M^+, 98).

$C_{10}H_8N_4O_2$ (216.2) Calcd. C 55.55 H 3.73 N 25.92
Found C 55.41 H 4.04 N 25.70

3d: Identical with the product obtained by the previous method, yield 86 mg (50%).

Ethyl 1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrido[2,3-d]pyrimidine-6-carboxylate **3e** was obtained from **2e** as light tan needles (diethyl ether), yield 47 mg (45%), m.p. 144–146°C. – IR (KBr): $\tilde{\nu}$ = 1760, 1720, 1670 cm^{-1} (CO). – ^1H NMR ($CDCl_3$): δ = 9.22 (d, 1H, 7-H, $J_{5,7}$ = 2.1 Hz), 8.97 (d, 1H, 5-H, $J_{5,7}$ = 2.1 Hz), 4.39 (q, 2H, CH_2, J = 6.4 Hz), 3.69 (s, 3H, NCH_3), 3.44 (s, 3H, NCH_3), 1.35 (t, 3H, CH_2CH_3, J = 6.4 Hz). – MS: *m/z* (%) = 263 (M^+, 82).

$C_{12}H_{13}N_3O_4$ (263.3) Calcd. C 54.75 H 4.98 N 15.96
Found C 54.53 H 5.26 N 15.84

3c *from Fumaronitrile:* 1.0 g (4.8 mmol) of uracil **1** and 0.40 g (5.0 mmol) of fumaronitrile were heated under reflux in 20 ml of acetonitrile for 12 h. The solvent was removed under reduced pressure and the residue subjected to column chromatography (silica gel) eluting with chloroform/acetone (9:1, v/v). The isolated product proved to be identical with the compound obtained by the previous method; yield 0.40 g (39%).

6-{[(Dimethylamino)methylene]amino}-5-(3,5-dioxo-4-phenyl-1,2,4-triazolin-1-yl)-1,3-dimethyluracil (**6a**): To a stirred solution of 1.0 g (4.8 mmol) of uracil **1** in 30 ml of anhydrous acetonitrile 0.80 g (4.8 mmol) of 4-phenyl-1,2,4-triazoline-3,5-dione (4-Ph-TAD) was added. The solution immediately became light yellow, and in less than 5 min a colorless precipitate began to form. Stirring was continued for an additional 2 h. The separated solid was filtered, and recrystallization from ethyl acetate gave the adduct as colorless amorphous solid; yield 1.3 g (71%), m.p. 203–204°C. – IR (KBr): $\tilde{\nu}$ = 3010 (NH), 1770, 1710, 1660 cm^{-1} (CO). – ^1H NMR ($CDCl_3$): δ = 10.55 (br. s, 1H, NH), 7.97 (s, 1H, CH), 7.3–7.7 (m, $5H_{arom.}$), 3.42 (s, 3H, NCH_3), 3.31 (s, 3H, NCH_3), 3.14, 3.09 [2 × s, 6H, $N(CH_3)_2$]. – ^{13}C NMR ($CDCl_3$): δ = 159.87 (C-8), 159.35 (C-7), 156.05 (C-16), 155.41 (C-2), 152.27 (C-6), 150.87 (C-4), 131.87 (C-9), 128.61 (C-11), 127.54 (C-12), 125.60 (C-10), 96.50 (C-5), 40.44, 34.28 (C-13, *E,Z* isomers), 30.40 (C-14), 27.52 (C-15). – MS: *m/z* (%) = 385 (M^+, 13).

$C_{17}H_{19}N_7O_4$ (385.4)
Calcd. (× 1/3 H_2O) C 52.17 H 5.07 N 25.04
Found C 52.51 H 5.06 N 24.70

5-[1,2-Bis(ethoxycarbonyl)hydrazino]-6-{[(dimethylamino)methylene]amino}-1,3-dimethyluracil (**6b**): 1.0 g (4.8 mmol) of uracil **1** and 0.90 g (5.0 mmol) of diethyl azodicarboxylate were heated under reflux in 20 ml of toluene for 8 h. The toluene was removed in vacuo affording a dark red oil. A small amount of ethyl acetate was added to the residue, the suspension cooled, and the separated product filtered. Recrystallization from ethyl acetate gave 1.1 g (60%) of the Michael adduct as a colorless amorphous solid; m.p. 106–107°C. – IR (KBr): = 2900 (NH), 1750, 1730, 1690 (CO), 1640–1600 br. cm^{-1} (C=N). – ^1H NMR ($CDCl_3$): δ = 8.28 (br. s, 1H, NH), 7.62 (s, 1H, CH), 4.11 (overlapping qu, 4H, OCH_2), 3.33 (s, 3H, NCH_3), 3.28 (s, 3H, NCH_3), 3.09 (s, 3H, $H_2C-N-CH_3$), 3.01 (s, 3H, $H_2C-N-CH_3$). – ^{13}C NMR ($CDCl_3$): δ = 161.87 (C-8), 157.83 (C-16), 156.56 (C-2), 155.79 (C-4,6), 151.58 (C-7), 102.38 (C-5), 63.28 (C-10), 61.53 (C-9), 40.78, 34.31 (C-13, *E,Z* isomers), 30.97 (C-14), 27.97 (C-15), 14.44 (C-11,12). – MS: *m/z* (%) = 384 (M^+, 28).

$C_{15}H_{24}N_6O_6$ (384.4) Calcd. C 46.87 H 6.29 N 21.87
Found C 47.12 H 6.33 N 21.97

5-[1,2-Bis(phenoxycarbonyl)hydrazino]-6-{[(dimethylamino)methylene]amino}-1,3-dimethyluracil (**6c**) was prepared in the same manner as **6b** from diphenyl azodicarboxylate affording the compound as a colorless amorphous solid from ethyl acetate; yield 0.84 g (35%), m.p. 184–185°C. – IR (KBr): $\tilde{\nu}$ = 2890 (NH), 1780, 1755, 1705, 1650 cm^{-1} (CO). – ^1H NMR ($CDCl_3$): δ = 8.39 (br. s, 1H, NH), 8.05 (br. s, 1H, N=CH), 7.0–7.4 (m, 10 $H_{arom.}$), 3.42 (s, 3H, NCH_3), 3.34 (s, 3H, NCH_3), 3.10 and 3.01 [2 × br. s, 6H, $N(CH_3)_2$]. – MS: *m/z* (%) = 480 (M^+, 10).

$C_{23}H_{24}N_6O_6$ (480.5) Calcd. C 57.49 H 5.04 N 17.49
Found C 57.49 H 5.14 N 17.33

8-(Dimethylamino)theophylline (**7**): 0.50 g (1.3 mmol) of the Michael adduct **6b** was heated in 3 ml of nitrobenzene between 190 and 200°C for 1.5 h. The solution was cooled to +10°C for ca. 12 h precipitating a colorless solid. A small amount of diethyl ether was added and the solution filtered. This afforded 0.10 g (34%) of **7** as a colorless solid; m.p. 335–337°C (ref.[14] >330°C). – IR (KBr): $\tilde{\nu}$ = 3300–3050 (NH), 1710, 1160 cm^{-1} (CO). – ^1H NMR ($CDCl_3$): δ = 11.30 (s, 1H, NH), 3.56 (s, 3H, NCH_3), 3.38 (s, 3H, NCH_3), 3.19 [s, 6H, $N(CH_3)_2$]. – MS: *m/z* (%) = 223 (M^+, 100).

Similar treatment of **6b** also resulted in the isolation of **7**, yield 0.15 g (53%). Although **6a** afforded also **7**, the pure material could not be isolated from the reaction mixture. High-resolution MS: exact mass calcd. for $C_9H_{13}N_5O_2$ = 223.1069; found 223.1070.

6-[2-(Dimethylamino)vinyl]-1,3-dimethyluracil (**8**): 3.1 g (20 mmol) of 1,3,6-trimethyluracil (**12**) and 4.5 g (35 mmol) of dimethylformamide dimethyl acetal were heated to 105°C in 10 ml of anhydrous DMF for 12 h. Then the reaction mixture was cooled to –10°C for ca. 12 h and the separated product filtered. Recrystallization from methanol gave the product as 2.9 g (69.4%) very pale yellow prisms; m.p. 189–190°C. – ^1H NMR ($CDCl_3$): δ = 7.00 (d, 1H, CH, J = 12 Hz), 5.53 (s, 1H, 5-H), 4.66 (d, 1H, CH, J = 12 Hz), 3.38 (s, 3H, NCH_3), 3.28 (s, 3H, NCH_3), 2.88 [s, 6H, $N(CH_3)_2$]. – IR (KBr): $\tilde{\nu}$ = 1680, 1650–1610 br. cm^{-1} (CO). – MS: *m/z* (%) = 209 (M^+, 100).

$C_{10}H_{15}N_3O_2$ (209.3) Calcd. C 57.40 H 7.23 N 20.08
Found C 57.75 H 7.40 N 20.24

Cycloaddition of **8** *to Electron Deficient Olefins*

Dimethyl 1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxo-5,6-quinazolinedicarboxylate (**9b**): 1.0 g (4.8 mmol) of the vinyluracil **8** and 0.70 g (4.8 mmol) of dimethyl fumarate were heated to reflux in 40 ml of anhydrous toluene for 16 h. Then the toluene was distilled off in vacuo affording a gummy pale yellow solid. Diethyl ether/ethyl acetate (1:1) (30 ml) was added and the suspension scratched vigorously. This resulted in the separation of a colorless solid which was filtered. Recrystallization from chloroform/hexane afforded the quinazoline as colorless irregular prisms; yield 0.30 g (20%), m.p. 209–210°C. – IR (KBr): $\tilde{\nu}$ = 1730, 1720, 1655 cm^{-1} (CO). – ^1H NMR ($CDCl_3$): δ = 8.35 (d, 1H, 8-H, $J_{7,8}$ = 7 Hz), 7.32 (d, 1H, 7-H, $J_{7,8}$ = 7 Hz), 4.05 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.63 (s, 3H, NCH_3), 3.43 (s, 3H, NCH_3). – MS: *m/z* (%) = 306 (M^+, 42).

$C_{14}H_{14}N_2O_6$ (306.3) Calcd. C 54.90 H 4.61 N 9.15
Found C 54.75 H 4.62 N 9.05

The following compounds were obtained by this method:

6-Acetyl-1,3-dimethyl-2,4(1H,3H)-quinazolinedione (**9a**): Colorless microneedles (ethyl acetate), yield 0.85 g (46%), m.p. 197°C. – IR (KBr): $\tilde{\nu}$ = 1710, 1680, 1660 cm^{-1} (CO). – ^1H NMR ($CDCl_3$): δ = 8.77 (d, 1H, 5-H, $J_{5,7}$ = 1.4 Hz), 8.31 (dd, 1H, 7-H, $J_{7,8}$ = 7.2, $J_{5,7}$ = 1.4 Hz), 7.27 (d, 1H, 8-H, $J_{7,8}$ = 7.2 Hz), 3.63 (s, 3H, NCH_3), 3.53 (s, 3H, NCH_3), 2.64 (s, 3H, $COCH_3$). – MS: *m/z* (%) = 232 (M^+, 48).

$C_{12}H_{12}N_2O_3$ (232.2) Calcd. C 62.06 H 5.21 N 12.06
Found C 61.94 H 5.18 N 12.12

Diethyl 1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxo-5,6-quinazolinedicarboxylate (**9c**): From diethyl fumarate or diethyl maleate in 32 and 31% yields, respectively, as light tan irregular prisms; m.p. 149–150°C (dichloromethane/diethyl ether). – IR (KBr): $\tilde{\nu}$ = 1740, 1720, 1660 cm^{-1} (CO). – ^1H NMR ($CDCl_3$): δ = 8.33 (d, 1H, $J_{7,8}$ = 4 Hz), 7.30 (d, 1H, 7-H, $J_{7,8}$ = 4 Hz), 4.65–4.22 (overlapping qu, 4H, 2 × CH_2CH_3), 3.58 (s, 3H, NCH_3), 3.42 (s, 3H, NCH_3), 1.43–1.23 (overlapping t, 6H, 2 × CH_2CH_3). – MS: *m/z* (%) = 334 (M^+, 22).

$C_{16}H_{18}N_2O_6$ (334.3) Calcd. C 57.48 H 5.43 N 8.38
Found C 57.06 H 5.31 N 8.21

Methyl 1,2,3,4,6,7-Hexahydro-1,3-dimethyl-2,4-dioxo-6-quinazolinecarboxylate (**10**): 1.0 g (4.8 mmol) of uracil **8** and 0.50 g (5.8 mmol) of methyl acrylate were heated to reflux in 30 ml of anhydrous toluene for 8 h. The reaction mixture was cooled to room temp. and the separated material filtered. Column chromatography (silica gel) of the solid eluting with ethyl acetate isolated the hexahydro adduct **10** as colorless microneedles; yield 0.20 g (17%); m.p. 215–217°C (ethyl acetate/hexane). – IR (KBr): $\tilde{\nu}$ = 1720, 1700, 1650 cm^{-1} (CO). – ^1H NMR ($CDCl_3$): δ = 6.89 (m, 1H, 6-H, $J_{5,6}$ = 4.0, $J_{6,7}$ = 2.0 Hz), 3.78 (s, 3H, OCH_3), 3.47 (s, 3H, NCH_3), 3.37 (s, 3H, NCH_3), 3.41–3.34 (m, 4H, 5,8-H, 7,7-H, $J_{5,6}$ = 4.0, $J_{6,7}$ = 2.0, $J_{7,8}$ = 5.8 Hz). – MS: *m/z* (%) = 250 (M^+, 78).

$C_{12}H_{14}N_2O_4$ (250.3) Calcd. C 57.59 H 5.64 N 11.20
Found C 57.87 H 5.56 N 11.20

Methyl 3-[3-(Dimethylamino)vinyl]-2,4,5,6-tetrahydro-2,5-dimethyl-1,4,6-trioxo-1H-pyrrolo[3,4-c]pyridine-7-carboxylate (**11**) was obtained using the same procedure as **5** above from **1**. Brown microneedles with an orange reflection, yield 0.61 g (48%), m.p. 319–324°C (ethyl acetate/ethanol). – IR (KBr): $\tilde{\nu}$ = 1720, 1660, 1650 cm^{-1} (CO). – ^1H NMR ([D_6]DMSO): δ = 3.71 (s, 3H, OCH_3), 3.55–3.20 [complex m, 11H, 2 × CH, $N(CH_3)_2$, NCH_3], 3.10 (s, 3H, NCH_3). – MS: *m/z* (%) = 319 (M^+, 100).

$C_{15}H_{17}N_3O_5$ (319.3) Calcd. C 56.42 H 5.36 N 13.16
Found C 56.36 H 5.44 N 13.01

1,3-Dimethyluracil-6-carbaldehyde Dimethylhydrazone (**14**): A mixture of 2.3 g (15 mmol) of 1,3,6-trimethyluracil (**12**) and 1.8 g (16 mmol) of finely ground selenium dioxide was heated at 100°C in 75 ml of glacial acetic acid for 4 h. Selenium deposited during the reaction, and the mixture was filtered while hot through a sintered glass funnel. The residue was washed with an additional amount of acetic acid (50 ml). The filtrate was concentrated to ca. 20 ml under reduced pressure, and the aldehyde thus formed was not purified[17] further. The mixture was suspended in 150 ml of distilled water, heated to 60–70°C and added dropwise over a 30-min period to a stirred solution of 1.0 g (16 mmol) of *N,N*-dimethylhydrazine in 200 ml of distilled water. After the addition was complete the mixture was heated to 70°C for 2 h during which a clear solution was obtained. The solution was cooled to room temp. and extracted with 3 × 200 ml of chloroform. The combined organic layers were washed with 2 × 100 ml of water, dried with sodium sulfate, and evaporated. Column chromatography (silica gel) of the residue eluting with chloroform afforded the hydrazone **14** as golden microneedles; yield 0.90 g (29%); m.p. 165–166°C (dichloromethane/hexane). – IR (KBr): $\tilde{\nu}$ = 1680, 1640 cm^{-1} (CO). – ^1H NMR ($CDCl_3$): δ = 6.64 (s, 1H, CH), 6.04 (s, 1H, 5-H), 3.54 (s, 3H, NCH_3), 3.33 (s, 3H, NCH_3), 3.12 [s, 6H, $N(CH_3)_2$]. – MS: *m/z* (%) = 210 (M^+, 100). – High-resolution MS: exact mass calcd. for $C_9H_4N_4O_2$ *m/z* = 210.1116; found 210.1113 (due to decomposition on storage no elemental analysis could be made).

Methyl 3-[(Dimethylhydrazono)methyl]-2,4,6-tetrahydro-2,5-dimethyl-1,4,6-trioxo-1H-pyrrolo[3,4-c]pyridine-7-carboxylate (**15**) was obtained from **14** using the same procedure as above for **8**. Purple irregular prisms, yield 0.32 g (27%), m.p. 205–206°C (ethyl acetate). – IR (KBr): $\tilde{\nu}$ = 1735, 1670 (CO), 1565 cm^{-1} (C=N). – ^1H NMR ($CDCl_3$): δ = 8.14 (s, 1H, CH), 3.91 (s, 3H, OCH_3), 3.48 (s, 3H, NCH_3), 3.45 (s, 3H, NCH_3), 3.29 [s, 6H, $N(CH_3)_2$]. – MS: *m/z* (%) = 320 (M^+, 65).

$C_{14}H_{16}N_4O_5$ (320.3) Calcd. C 52.49 H 5.04 N 17.49
Found C 52.36 H 5.11 N 17.14

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1: 120788-53-6 / **2a**: 120788-54-7 / **2b**: 120788-64-9 / **2c**: 120788-65-0 / **2d**: 120788-66-1 / **2e**: 120788-67-2 / **3a**: 120788-55-8 / **3b**: 120788-68-3 / **3c**: 120788-69-4 / **3d**: 120788-71-8 / **3e**: 120788-70-7 / **5**: 120788-56-9 / **6a**: 120788-57-0 / **6b**: 120788-72-9 / **6c**: 120788-73-0 / **7**: 5426-47-1 / **8**: 120788-58-1 / **9a**: 120788-59-2 / **9b**: 120788-74-1 / **9c**: 120788-75-2 / **10**: 120788-60-5 / **11**: 120788-61-6 / **12**: 13509-52-9 / **14**: 120788-62-7 / **15**: 120788-63-8 / $CH_2=CHCOCH_3$: 78-94-4 / $CH_2=CHCO_2CH_3$: 96-33-3 / $CH_2=CHCN$: 107-13-1 / (*E*)-$CH_3O_2CCH=CHCO_2CH_3$: 624-49-7 / (*E*)-$EtO_2CCH=CHCO_2Et$: 623-91-6 / (*Z*)-$CH_3O_2CCH=CHCO_2CH_3$: 141-05-9 / (*Z*)-$EtO_2CCH=CHCO_2Et$: 624-48-6 / $NCCH=CHCN$: 764-42-1 / 4-Ph-TAD: 4233-33-4 / $EtO_2CN=NCO_2Et$: 1972-28-7 / $PhO_2CN=NCO_2Ph$: 2449-14-1 / 6-amino-1,3-dimethyluracil: 6642-31-5

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[1] Preliminary publication: E. B. Walsh, H. Wamhoff, *Tetrahedron Lett.* **29** (1988) 4401. – Part 15: H. Wamhoff, J. Muhr, *Synthesis* **1988**, 919.

[2] Reviews on this subject, cf.: [2a] E. Lutz, C. G. Newton, *Comprehensive Heterocyclic Chemistry* (A. R. Katritzky, C. W. Rees, Eds.), Vol. 3 (A. J. Boulton, A. McKillop, Eds.), pp. 129–261, Pergamon Press, Oxford 1984. – [2b] E. M. Grivsky, S. Lee, C. W. Siegel, D. S. Duck, C. A. Nichol, *J. Med. Chem.* **23** (1980) 327. – [2c] G. Tamura, T. Sakaguchi, T. Kawasaki, Y. Kita, *Heterocycles* **3** (1975) 183; G. Bennett, W. Simpson, R. Mason, R. Strohshein, R. Mansukhani, *J. Org. Chem.* **42** (1977) 221; K. Nagahara, A. Takada, *Heterocycles* **9** (1978) 197; T. Itoh, H. Oguia, N. Kawahara, T. Nakajima, K. A. Watanabe, *ibid.* **20** (1983) 2177; T. Nagamatsu, M. Koga, F. Yoneda, *Chem. Pharm. Bull.* **32** (1984) 1699; J. B. Press, V. T. Bandurco, E. M. Wong, Z. G. Hajos, R. M. Kanojia, R. A. Mallory, E. G. Deegan, J. J. McNally, J. R. Roberts, M. L. Cotter, D. W. Graden, J. R. Lloyd, *J. Heterocycl. Chem.* **23** (1986) 1821.

[3] T. Kunieda, B. Witkop, *J. Am. Chem. Soc.* **93** (1971) 3478; H. P. M. Thiellier, G. J. Koomen, U. K. Pandit, *Heterocycles* **5** (1976) 19; *Tetrahedron* **33** (1977) 1493, 2603, 2609; S. Senda, T. Asao, I. Sugiyama, K. Hirota, *Tetrahedron Lett.* **21** (1980) 531; M. Noguchi, S. Nagata, S. Kajigaeshi, *Chem. Pharm. Bull.* **34** (1980) 3994.

[4] K. T. Potts, E. B. Walsh, *J. Org. Chem.* **53** (1988) 1199.

[5] B. Serckx-Poncin, A. Hesbain-Frisque, L. Ghosez, *Tetrahedron Lett.* **23** (1982) 3261; K. T. Potts, E. B. Walsh, D. Bhattacharjee, *J. Org. Chem.* **52** (1987) 2285; A. Waldner, *Helv. Chim. Acta* **71** (1988) 486, 493.

[6] A. Demoulin, H. Gorissen, A. Hesbain-Frisque, L. Ghosez, *J. Am. Chem. Soc.* **97** (1975) 4409.

[7] Determined by simple Hückel calculations in which the ω-technique was used to obtain self-consistency; cf. A. Streitwieser, *Molecular Orbital Theory for Organic Chemists*, p. 115, Wiley,

New York 1961; we thank Prof. Dr. *K. T. Potts* and Dr. *P. Murphy*, Rensselaer Polytechnic Institute, Troy, NY, for these calculations.

[8] H. C. S. Woods, R. Wriggleswork, D. A. Yeowell, F. W. Gurney, B. S. Hurlbert, *J. Chem. Soc., Perkin Trans 1*, **1974**, 1225.

[9] Cf. R. H. F. Manske, M. Kulka, *Org. Reactions* **7** (1953) 59; R. Stewart, *Oxidation Mechanisms, Application to Organic Chemistry*, p. 114, Benjamin, New York 1964; Y. Ogata, J. Mibae, *J. Org. Chem.* **27** (1962) 2048.

[10] H. Wamhoff, W. Schupp, A. Kirfel, G. Will, *J. Org. Chem.* **51** (1986) 149; H. Wamhoff, W. Schupp, *ibid.* **51** (1986) 2787.

[11] For X-ray crystal data cf. ref.[1].

[12] E. C. Taylor, F. Sowinski, *J. Org. Chem.* **39** (1974) 903; F. Yoneda, Y. Sakuma, T. Nagamatsu, S. Mizumoto, *J. Chem. Soc., Perkin Trans. 1*, **1976**, 2398.

[13] H. Wamhoff, K. Wald, *Org. Prep. Proc. Int.* **7** (1975) 251; cf. M. Fieser, L. F. Fieser, *Reagents for Organic Synthesis*, Vol. 6, pp. 75–76, Wiley-Interscience, New York 1977; H. Wamhoff, G. Kunz, *Angew. Chem.* **93** (1981) 832; *Angew. Chem. Int. Ed. Engl.* **20** (1981) 797.

[14] F. Yoneda, T. Nagamatsu, *J. Am. Chem. Soc.* **96** (1974) 5607; F. Yoneda, M. Higuchi, S. Matsumoto, *J. Chem. Soc., Perkin Trans. 1*, **1977**, 1754; F. Yoneda, M. Kawamura, S. Matsumoto, M. Higuchi, *ibid.* **1977**, 2285.

[15] F. Yoneda, M. Higuchi, T. Matsumoto, K. Senga, *Bull. Chem. Soc. Jpn.* **46** (1973) 1836.

[16] Similar cycloadditions of **8** were described by S. Senda, K. Hirota, T. Asao, Y. Toyota, *Heterocycles* **12** (1979) 197.

[17] R. B. Silverman, M. P. Groziak, *J. Am. Chem. Soc.* **104** (1982) 6434.

[73/89]