Dihydropyrimidines and Related Structures. I. N^2-Substituted 2-Pyrimidinamines and Dihydro-2-pyrimidinamines by Reaction of Phenylbutenones and Monosubstituted Guanidines [1]

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The reactions of monosubstituted guanidines **2** with phenylbutenones **7** and **10** exclusively yield N^2-substituted 2-pyrimidinamines **8** and **9**. The structure of the reaction products is proved and their differing stability is discussed. Action of methyl- and benzylguanidine respectively (**2b, c**) on 4-phenyl-3-buten-2-one (**7**) and of **2c** on 1-phenyl-2-buten-1-one (**10**) under atmospheric oxygen affords aromatic N^2-substituted 2-pyrimidinamines **9b** and **c**. The dihydropyrimidines **8b** and **c**, probable intermediates of the reactions, could not be isolated. In contrast, heating of arylguanidines **2d, e** with **7** leads to stable dihydropyrimidinamines **8d** and **e**, which can be isolated as bases. Addition of methanol to **8d** yields 6-methoxy-2-pyrimidinamine **11d**, boiling of **8d** in DMF affords **9d**. Under nitrogen, guanidine adds to **7** to yield aminopyrimidinol **13a**, which is transformed by heating in benzene into pyrimidine **9a**. The low stability of **8a-c** is attributed to their strong basicity, the greater stability of **8d** and **e** to their lower basicity. The structural formulae of **8d, e** and **9b-d** and their salts respectively were established partly (**8e**) by nmr and partly (**9b-d**) by comparison of the corresponding picrates with authentic samples [17].

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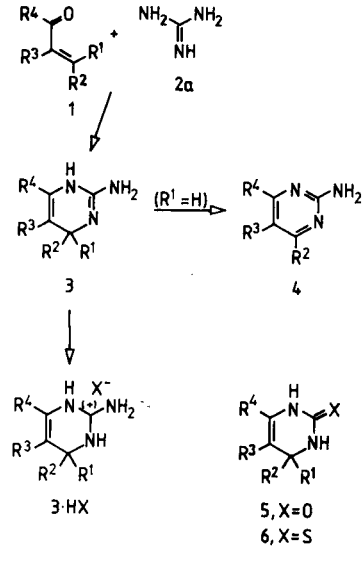
β,β-Disubstituted alkenones **1** are transformed by action of guanidine (**2a**) to yield stable dihydropyrimidinamines **3** [2-4]. In contrast, alkenones **1** with hydrogen in β-position condense with guanidine to afford mostly labile dihydropyrimidinamines **3**, which are frequently already during the reaction converted into aromatic pyrimidines **4** [5]. We have also found, an important observation, that unstable dihydropyrimidines **3** can often be stabilized by transformation into corresponding salts **3**·HX.

These findings agree with reports on dihydroheterocycles, which are stabilized by strongly electron-withdrawing substituents. For example, dihydropyrimidinones **5** and -thiones **6** with equal substitution to the above mentioned labile dihydropyrimidinamines **3** are stable against atmospheric oxygen, as are salts **3**·HX [6-8]. Similarly, 1,4-dihydropyridine is unstable [9], whereas dihydropyridines with electron-withdrawing groups such as 1,4-dihydronicotinamide [10], esters of 1,4-dihydronicotinic acid [11] and 1,4-dihydropyridine-3,5-dicarboxylic acid [12] or 1,4-dihydro-3,5-bis(phenylthio)-2,4,6-triphenylpyridine [13] are stable at room temperature.

Scheme I



Results and Discussion.

In this work, we are investigating, whether unstable dihydropyrimidinamines of type **3** can also be stabilized against atmospheric oxygen by introduction of electron-withdrawing substituents. As a basis for the comparisons the labile 1,4-dihydro-6-methyl-4-phenyl-2-pyrimidinamine (**8a**), the probable intermediate of the formation of pyrimidine **9a** from guanidine (**2a**) and 4-phenyl-3-buten-2-one (**7**), was employed. Up to now, **8a** could not be isolated, as it aromatizes during the reaction [5,14].

In order to study the influence of various substituents on the stability of the probably labile intermediate **8a**, phenylbutenone **7** was condensed with methyl-, benzyl-, phenyl and *p*-methoxyphenylguanidine (**2b-e**).

The action of methyl- and benzylguanidine respectively (**2b** and **c**) on phenylbutenone **7** in benzene with access of atmospheric oxygen in analogy to the reaction of guanidine (**2a**) with **7** [5] directly yields maximum unsaturated N^2-substituted 4-methyl-6-phenyl-2-pyrimidinamines **9b** and **c** (condensates **B** and **C**). Dihydropyrimidines **8b** and **c** could not be isolated. Heating of benzylguanidine with

1-phenyl-2-buten-1-one (**10**) also directly yields N^2-benzyl-2-pyrimidinamine **9c**. In both series **9b** and **c** were isolated as picrates.

In contrast, boiling of phenyl- and *p*-methoxyphenylguanidine respectively (**2d** and **e**) with 4-phenyl-3-buten-2-one (**7**) in benzene under atmospheric oxygen affords N^2,4-diphenyl- and N^2-(*p*-methoxyphenyl)-4-phenyl-1,4-dihydro-6-methyl-2-pyrimidinamine respectively (**8d** and **e** = condensates **D'** and **E'**). Contrary to earlier prepared dihydropyrimidinamines **3**, which, as a consequence of their low stability [5], could be isolated only as salts, **8d** and **e** are stable dihydro compounds. They can be isolated as bases and recrystallized without aromatization.

The 5,6-position of the (C=C) double bond in **8d** and **e** is established by nmr (coupling of C^4H and C^5H). It is, however, not possible to decide by means of nmr, whether **8d** and **e** are 1,4- or 1,6-dihydro-2-pyrimidinamines or 3,4-dihydro-2(1*H*)-pyrimidinimines in solution. The appearance of only one broad signal for the 2 NH-protons indicates that a rapid exchange of NH-protons takes place between these tautomeric compounds, compare [2]. As a substitute for the actual form, condensates **8** are called 1,4-dihydro-2-pyrimidinamines **8** in this report. For the signals of NH-protons in the spectra of salts **8**·HX see below.

Hot methanol adds to dihydropyrimidine **8d** to yield 6-methoxy-6-methyl-4-phenyl-1,4,5,6-tetrahydro-2-pyrimidinamine (**11d**). In contrast to pyrimidinol **13a** (see below), **11d** partly splits off methanol (but not hydrogen) on being heated in inert solvents to yield again dihydro compound **8d**.

Aromatization of the stable N^2-phenyldihydro-2-pyrimidinamine **8d** yielding pyrimidine **9d** takes place only under rough conditions, for example on heating **8d** in boiling tetramethylurea under atmospheric oxygen.

Parallel to the above described experiments, we also tried to condense phenylguanidine **2d** with **7** in DMF as solvent, but only a small amount of N^2,N^4-diphenyl-2,4-triazinediamine (**12**) could be isolated in this experiment. The product is formed by condensation of 2 molecules phenylguanidine **2d** with DMF, with phenylbutenone **7** not participating in the reaction [15].

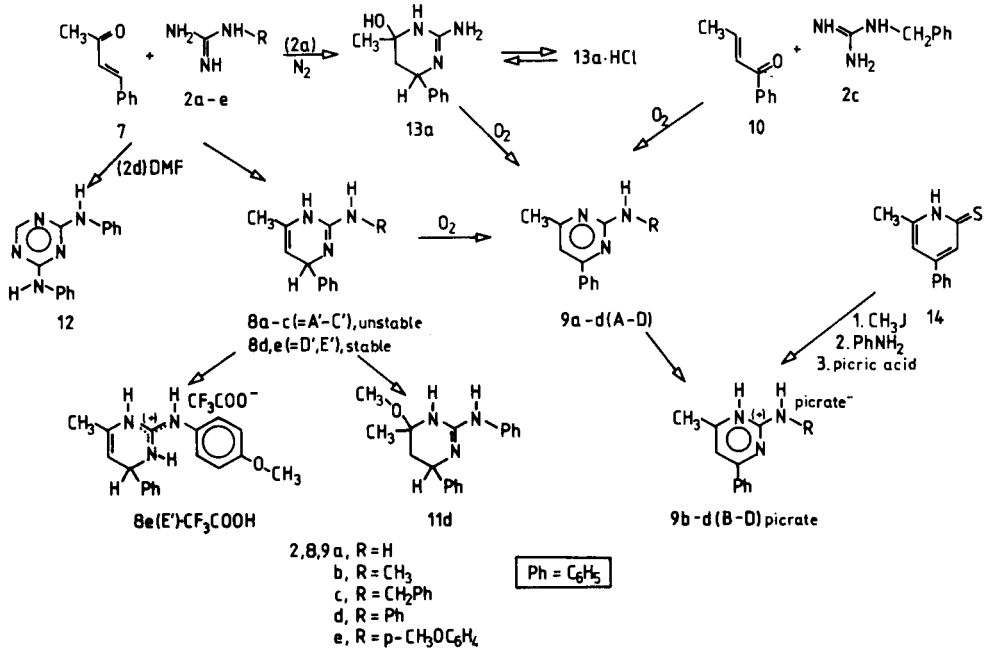
Efforts to prepare 6-methyl-4-phenyl-1,4-dihydro-2-pyrimidinamine (**8a**) under nitrogen atmosphere and/or at low temperatures were not successful, we could isolate only 2-amino-3,4,5,6-tetrahydro-4-methyl-6-phenyl-4-pyrimidinol hydrochloride (**13a**·HCl), an addition product. On boiling **13a** (base) in benzene under nitrogen atmosphere **13a** remained unchanged (no formation of dihydro compound **8a**), heating of **13a** under atmospheric oxygen yielded pyrimidinamine **9a** [14].

The quick formation of aromatic pyrimidines **9a-c** in the reaction of guanidines **2a-c** with butenone **7** [14] may be a consequence of the relatively strong basicity of the intermediates **8a-c**. The electron excess in the pyrimidine nucleus, resulting from resonance-donating substituents in 2-position (amino, methylamino, benzylamino), facilitates oxidation of **8a-c**.

In contrast, the greater stability of 2-phenylaminodihydropyrimidines **8d** and **e** may be attributed to the lower basicity of these compounds.

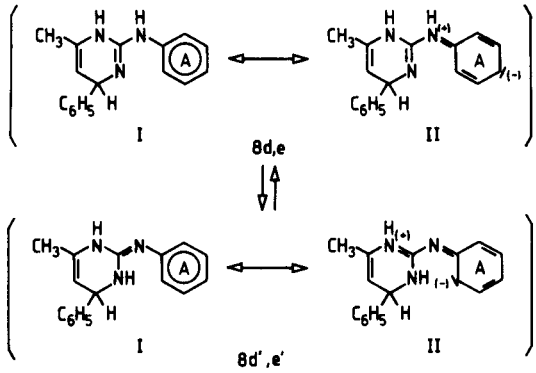
As can be seen by nmr (upfield shift of the *o*- and *p*-protons of phenyl radical A in comparison with the benz-

Scheme II



ene signal) the aryl radicals A withdraw electrons from the pyrimidine nucleus in accordance with resonance structures of type **8d, e** II and **8d′, e′** II (Scheme III). Just as the positive charge in stable salts of type **3**·HX [5], the thus generated electron deficiency in the pyrimidine ring impedes easy aromatization of **8d** and **e** (which is probably connected with the splitting off of hydride ions from C-4).

Scheme III



The above described reactions of phenylbutenones **7** and **10** respectively with monosubstituted guanidines **2** could yield *a priori* N^1- or N^2- or N^3-substituted 2-pyrimidinamines or -imines, but in accordance with earlier investigations [16,17] the isolated bases are exclusively N^2-substituted 2-pyrimidinamines **8** and **9** respectively. The preferred formation of pyrimidines **8** an **9** seems to be independent of the steric and electronic effects of the substituent R (methyl, benzyl, phenyl) in the monosubstituted guanidine.

The structural formulae of the pyrimidines **B** and **C** (prepared from methyl- and benzylguanidine respectively and benzalacetone **7** or ethylidenacetophenone **10**), and of pyrimidine **D** (formed by oxydation of dihydropyrimidine **D′**, which had been prepared from **7** and phenylguanidine) were proved by comparing their picrates with authentic samples of **9b,c** and **d** picrate [17,15]. As the picrates are identical, **B-D** are N^2-substituted 2-pyrimidinamines **9b-d**, and consequently dihydro compound **D′**, being the preceding stage of **D** must be 6-methyl-N^2,4-diphenyl-1,4-dihydro-2-pyrimidinamine (**8d**).

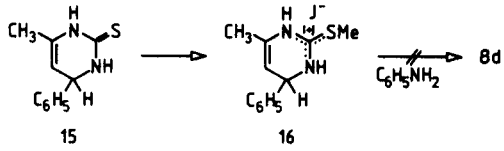
Authentic samples of **9b** and **9c** picrate were at our disposal from earlier investigation [17], they had been prepared from guanidines **2b** and **c** and 1-phenyl-1,3-butanedione *via* N^2-methyl- and N^2-benzyl-2-pyrimidinamine **9b** and **c**. The sructures of **9b** and **c**, and at the same time the structures of their picrates, had been proved by nmr (coupling of the amine protons of **9b** and **9c** base with the neighbouring methyl and benzyl protons).

We also tried to establish by nmr the N^2-position of methyl and benzyl group directly for **9b** and **9c** picrate (coupling of the NH- with the neighbouring methyl and benzyl protons would have proved the N^2-position of the substituents and would not have been consistent with the N^1- or N^3-position of the substituent in isomeric salts). However, in the spectra of **9b** and **9c** picrate, there appear only singlets for the methyl and benzyl protons respectively and this finding does not allow to determine the position of the substituent at N^1, N^2 or N^3, compare [16].

Authentic **9d** picrate had been prepared in the course of preceding research [17] starting from 6-methyl-4-phenyl-2(1*H*)-pyrimidinethione (**14**) [18] *via* corresponding 2-methylthiopyrimidinium iodide and by treatment of the latter first with aniline and then with picric acid.

Efforts to analogously synthetize 2-phenylamino- and 2-(*p*-methoxyphenylamino)dihydropyrimidine **8d** and **e** respectively starting from dihydropyrimidinethione **15** [6] *via* methylthiopyrimidine hydroiodide **16** failed. Action of aniline and *p*-methoxyaniline respectively on **16** effected its decomposition. Accordingly, it was not possible to isolate **8d** and **e** respectively.

Scheme IV



Frequently, the structure of N^2-monosubstituted dihydro-2-pyrimidinamines of type **8** can also be established by means of nmr spectra of corresponding salts **8**·HX. These salts (see Scheme II) are cyclic guanidinium ions with one substituent and one hydrogen atom attached to each of the three nitrogen atoms. The N^2-position of the substituent is proved, if three distinct nmr signals each with intensity one, appear for the three protons attached to N^1, N^2 and N^3 [16].

Unfortunately, we were not able to prepare picrates of **D′** (= **8d**) (partial addition of ethanol) and **E′** (= **8e**). However, the nmr method could be applied successfully to the establishment of the structure of condensate **E′**, when we prepared its trifluoroacetate directly in deuteriochloroform solution and took nmr spectra at +36°, 0°, −15°, −30° and −50°. At +36°, three singlets with intensity one each appeared for the three NH protons, indicating that **E′**·CF_3COOH is N^2-(*p*-methoxyphenyl)-2-pyrimidinamine trifluoroacetate **8e**·CF_3COOH with one proton at each of the three nitrogen atoms (the finding is not consistent with the structures of isomeric N^1- or N^3-methoxyphenyl-2-pyrimidinamine).

In recent experiments, we also investigated the influence of electron-withdrawing and electron-donating substituents in 4- and 6-position of dihydropyrimidinamines **3** on their stability. A report on this research will soon be published [19].

EXPERIMENTAL

Melting points were determined on a Kofler melting point apparatus. Thin-layer chromatograms were run on Polygram SIL G/UV 254-plates (Macherey-Nagel and Co). Elution solvent I (e.s. I): chloroform-methanol-glacial acetic acid 90:30:5; e.s. II: benzene-methanol 80:20; e.s. III: benzene-methanol 90:10. The developed spots were detected by visual examination under uv light. Infrared spectra were recorded with a Perkin-Elmer 225 grating-spectrophotometer. Nuclear magnetic resonance spectra were taken on a Perkin-Elmer R 32 instrument. Chemical shifts are reported as δ-units (ppm) with sodium-trimethylsilylpropanesulfonate or tetramethylsilane as an internal standard. Mass spectra were obtained using a Varian-311A spectrometer (EI, 70 eV, R 1000). Elemental analyses were performed by Institute of Organic Chemistry, Graz, Austria.

1,4-Dihydro-6-methyl-*N*²,4-diphenyl-2-pyrimidinamine (**8d**).

A stirred mixture of 4.05 g (0.03 mole) of phenylguanidine (**2d**) and 3.39 g (0.03 mole) of 4-phenyl-3-buten-2-one (**7**) in 100 ml of benzene was heated in a 250 ml Erlenmeyer flask fitted with water separator, reflux condenser and sodalime drying tube until the separation of water was finished (6 hours). After evaporating to a volume of 20 ml *in vacuo* and standing for 3 days the reaction mixture had set off crude **8d**. Washing with cold benzene and recrystallization from ethyl acetate yielded 2.2 g (28%) of **8d**, colourless needles, mp 125°, tlc (e.s. I), Rf = 0.58; ir (potassium bromide): 3390 (NH_2), 1695 (C=C-N), 1650 (C=N, NH_2), 1590, 1455, 830, 695 cm^{-1}; nmr (deuteriochloroform): δ 1.78 (s, CH_3, 3H), 4.58 (d, H-4, 1H, $J_{4,5}$ = 5 Hz), 5.00 (d, H-5, 1H), 7.32 (broad, aromatic and NH, 12H).

Anal. Calcd. for $C_{17}H_{17}N_3$: C, 77.53; H, 6.51; N, 15.96. Found: C, 77.27; H, 6.67; N, 16.08.

According to tlc, **8d** is also furnished by heating methoxytetrahydropyrimidine **11d** in benzene or DMSO-d_6.

1,4-Dihydro-*N*²-(4-methoxyphenyl)-6-methyl-4-phenyl-2-pyrimidinamine (**8e**).

A mixture of 8.26 g (0.05 mole) of 4-methoxyphenylguanidine (**2e**) and 7.31 g (0.05 mole) of **7** in 100 ml of benzene was treated and worked up as described for the preparation of **8d**. Recrystallization of the crude product from ethyl acetate yielded 5 g (34%) of **8e**, colourless needles, mp 166°, tlc (e.s. II), Rf = 0.35; ir (potassium bromide): 3400, 3380 (NH_2, NH), 1695 (C=C-N), 1650 (C=N, NH_2), 1340, 1225, 850 cm^{-1}; nmr (deuteriochloroform): δ 1.55 (s, CH_3-6 3H), 3.76 (s, CH_3O, 3H), 4.42 (d, H-4, 1H, $J_{4,5}$ = 4 Hz), 4.90 (d, H-5, 1H), 6.86 (broad, methoxyphenyl, 4H), 7.30 (broad, phenyl, 5H); ms: m/e 293 (M^+, 56), 291 (M^+-2 = **9e**$^+$, 100), 276 (M^+-17 = **9e**$^+-15$, 72), 146 (M^+-147, 73).

Anal. Calcd. for $C_{18}H_{19}N_3O$: C, 73.70; H, 6.53; N, 14.32. Found: C, 73.81; H, 6.25; N, 14.23.

NMR of **8e**·CF_3COOH (at +36°).

The solution was prepared by adding trifluoroacetic acid to the solution of **8e** in deuteriochloroform; only the signals of NH protons are reported: 6.11 (s, 1H), 7.55 (s, 1H), 8.50 (s, 1H); at lower temperatures (0°, −15°, −30°, −50°) two of the three NH-signals become broad and indistinct.

*N*²,4-Dimethyl-6-phenyl-2-pyrimidinamine Picrate (**9b** Picrate).

A stirred solution of 3.66 g (0.05 mole) of **2b** and 7.31 g (0.05 mole) of **7** in 100 ml of benzene was heated for 5 hours as described for the synthesis of **8d**. After cooling, the reaction-mixture was adjusted to *p*H 6 with 2*N* ethanolic hydrochloric acid. The solvent was evaporated *in vacuo* and the dark residue treated with 50 ml of 2*N* aqueous sodium hydroxide. The resulting mixture was extracted twice with 50 ml of ether each. The combined ether layers were evaporated *in vacuo*, yielding 9 g of a brown residue. One g of the latter and 1.3 g of picric acid were each dissolved in 10 ml of ethanol. Heating of the combined solutions, cooling, filtering, and washing of the precipitate with hot ethanol yielded 0.5 g (21%, calculated for the total charge) of **9b** picrate, yellow sticks, mp 270°, identical (mp, ir, nmr) with authentic **9b** picrate, mp 270° [17].

*N*²-Benzyl-4-methyl-6-phenyl-2-pyrimidinamine Picrate [**9c** Picrate, From **2c** and 4-Phenyl-3-buten-2-one (**7**)].

A stirred solution of 3.2 g (0.0215 mole) of **2c** and 3.14 g (0.0215 mole) of **8** in 50 ml of benzene was heated 1 hour as described for the preparation of **8d**. The reaction mixture was neutralized with 2*N* ethanolic hydrochloric acid and evaporated to dryness *in vacuo*. The dark residue, dissolved in 20 ml of ethanol, was transformed into **9c** picrate with 3.5 g (0.0153 mole) of picric acid as described in the preceding experiment. Washing of the crude picrate with hot ethanol yielded 1 g (9%) of **9c** picrate, yellow crystals, mp 248°, identical (mp, ir, nmr) with authentic **9c** picrate, mp 248° [17].

9c Picrate [From **2c** and 1-Phenyl-2-buten-1-one (**10**)].

A mixture of 5.96 g (0.04 mole) of **2c** and 5.84 g (0.04 mole) of **10** was placed in a 20 ml flask sealed with a sodalime tube and stirred at 130° (oil bath) for 2 hours. Two tenths (2.0 g) of the resulting dark mass was dissolved in 15 ml of ethanol and treated with 2.1 g (0.009 mole) of picric acid as described for the preparation of **9b** picrate to yield 1.1 g (27%, calculated for the total charge) **9c** picrate, mp 248°, identical with **9c** picrate, prepared from **2c** and **7** (see preceding experiment).

4-Methyl-*N*²,6-diphenyl-2-pyrimidinamine Picrate (**9d** Picrate) [15].

A solution of 1.5 g (0.0064 mole) of dihydropyrimidine **8d** (preparation see above) in 25 ml of tetramethylurea was heated under reflux for 5 hours. After evaporation of the solvent *in vacuo* 1.4 g of a brown residue remained. A solution of 0.4 g of the residue in 5 ml of ethanol was transformed into **9d** picrate with 1.15 g (0.005 mole) of picric acid as described for the preparation of **9b** picrate. Washing of the crude salt with hot ethanol yielded 0.3 g (67%, calcd. for the total charge) of **9d** picrate, yellow crystals, mp 267°, identical (mp, ir, nmr) with authentic **9d** picrate, mp 267° [17].

1,4,5,6-Tetrahydro-6-methoxy-6-methyl-*N*²-,4-diphenyl-2-pyrimidinamine (**11d**, From **8d**).

A solution of 0.1 g (0.0038 mole) of **8d** in 5 ml of methanol was refluxed for 5 minutes. After cooling, the crude product was filtered and recrystallized from methanol to yield 0.08 g (71%) of **11d**, colourless needles, mp 158°, tlc (e.s. I), Rf = 0.74; ir (potassium bromide): 3390, 3170 (NH_2, NH), 1645 (C=N, NH_2), 1585, 1480, 1440 cm^{-1}; nmr (DMSO-d_6; on dissolving, about 75% of **11d** are transformed into **8d**), signals for **11d**: δ 1.38 (s, CH_3, 3H), 2.21 (broad, CH_2, 2H), 3.48 (broad, CH_3O, 3H), 7.32 (broad, aromatic, 10H); ms: m/e 295 (M^+, 63), 263 (M^+-32 = **8d**$^+$, 88), 262 (M^+-33, 100).

Anal. Calcd. for $C_{18}H_{21}N_3O \cdot 0.15H_2O$: C, 72.52; H, 7.20; N, 14.10. Found: C, 72.51; H, 7.22; N, 14.15.

Compound **11d** (From **7** and **2d**).

A mixture of 4.05 g (0.03 mole) of **2d** and 3.39 g (0.03 mole) of **7** in 100 ml of benzene was treated as described for preparing **8d**. The solvent was evaporated *in vacuo* and the residue dissolved with stirring in 20 ml of methanol. After 24 hours the thus generated precipitate (according to tlc **8d** and **11d**) was filtered and refluxed in 20 ml of methanol for 12 hours. After cooling **11d** was filtered, yield 2.3 g (36%), mp 158°, identical (mp, ir, tlc) with the above described base **11d**.

*N*²,*N*⁴-Diphenyl-2,4-triazinediamine (**12**) [15].

In a flask with reflux condenser and water separator, a solution of 4.38 g (0.03 mole) of **7** and 4.05 g (0.03 mole) of phenylguanidine (**2d**) in 50 ml of dimethylformamide was heated with stirring at 110° for 17 hours. After evaporation of the solvent *in vacuo* to a volume of 10 ml, crystals precipitated, which were filtered and recrystallized from glacial acetic acid to yield 0.3 g (8%) of **12**, colourless needles, mp >300°; ir (potassium bromide): 3260, 3180 (NH), 1643 (C=N), 1580, 1530, 810, 753 cm^{-1}; nmr (DMSO-d_6): δ 7.10 (t, 4'-H, of $2C_6H_5$, 2H), 7.38 (t, 3'-H, and 5'-H of $2C_6H_5$, 4H, $J_{2',3'}$ = $J_{3',4'}$ = 8 Hz), 7.83 (d, 2'-H and 6'-H of $2C_6H_5$, 4H), 8.42 (s, H-6, 1H).

Anal. Calcd. for $C_{15}H_{13}N_5$: C, 68.43; H, 4.96; N, 26.60. Found: C, 68.54; H, 5.32; N, 26.38.

2-Amino-3,4,5,6-tetrahydro-4-methyl-6-phenyl-4-pyrimidinol Hydrochloride (**13a**·HCl).

A mixture of 40.6 g (0.278 mole) of **7**, 16.4 g (0.278 mole) of guanidine and 100 ml of benzene was heated under nitrogen-atmosphere for 1.5 hours as described for the preparation of **8d**. The reaction mixture was extracted with 100 ml of 4*N* aqueous hydrochloric acid. The aqueous layer was separated and evaporated to dryness *in vacuo*. The residue was treated with ethyl acetate to yield 6 g of crude **13a**·HCl. Repeated treating of the latter with small quantities of cold water gave 3.8 g (6%) of **13a**·HCl, colourless needles, mp 147°, tlc (e.s. I), Rf = 0.17; ir (potassium bromide): 3320 (NH_2), 3130-2700, 1670 (C=N, NH_2), 1615, 1135, 965 cm^{-1}; nmr (DMSO-d_6): δ 1.52 (s, CH_3, 3H); C^5H_2 and C^6H (ABX-system, $J_{ab} = J_{ac} = 13$ Hz, $J_{bc} = 5$ Hz), 1.79 (t, proton a), 2.13 (dd, proton b), 4.80 (dd, proton c), 7.45 (s, aromatic, 5H), 7.3-9.0 (broad, NH_2, 2NH, OH, 5H).

Anal. Calcd. for $C_{11}H_{16}ClN_3O$: C, 54.66; H, 6.67; Cl, 14.67; N, 17.38. Found: C, 54.88; H, 6.64; Cl, 14.81; N, 17.38.

1,4-Dihydro-6-methylthio-2-methyl-4-phenylpyrimidine Hydrochloride (**16**·HI).

A mixture of 11.5 g (0.056 mole) of dihydropyrimidinethione **15** [6], 23.8 g (0.168 mole) of methyl iodide and 700 ml of chloroform was stirred for 17 hours at room temperature. As about 50% of **15** had not reacted (tlc), the reaction-mixture was evaporated *in vacuo* to a volume of 150 ml and another 23.8 g (0.168 mole) of methyl iodide were added. Then the mixture was stirred for 2 hours at 50°. The solvent was removed and the residue dried for 16 hours at 100°. Treating of the resulting product with dioxane yielded 16.5 g of crude **16**·HI, recrystallization of the latter from acetone and washing of the obtained crystals with dioxane and ether gave 12.5 g (57%) of colourless rods, mp 127°, tlc (e.s. III), Rf = 0.32.

Salt **16**·HI crystallizes with half a mole of dioxane, which cannot be removed by drying *in vacuo* without decomposition. The dioxane of crystallization can also be seen by nmr. In any case, the molecular weight of the base **16** is proved by ms; ir (potassium bromide): 3300, 3240, 3160 (NH), 1698 (C=C-N), 1595, 1532, 1205 cm^{-1}; nmr (DMSO-d_6): δ 1.90 (s, CH_3-6, 3H), 2.73 (s, CH_3-S, 3H), 3.56 (s, CH_2-dioxane, 4H), 5.12 (d, H-4, 1H, $J_{4,5} = 6$ Hz), 5.45 (d, H-5, 1H), 7.40 (s, aromatic, 5H), 15.0-16.0 (broad, NH, 2H); ms: m/e 218 (M^+, 18), 204 ($M^+ - 14$, 85), 142 ($M^+ - 76$, 100), 88 (dioxane$^+$, 10).

Anal. Calcd. for $C_{12}H_{15}JN_2S \cdot 0.5\ C_4H_8O_2$ (dioxane): C, 43.08; H, 4.91; N, 7.18; S, 8.21. Found; C, 43.03; H, 5.21; N, 7.02; S, 8.41.

Salt **16**·HI was also prepared by refluxing a mixture of 9.5 g (0.045 mole) of **15**, 7.67 g (0.054 mole) of methyl iodide and 400 ml of acetone for 0.45 hours. Removing of the solvent *in vacuo* and treating of the residue with dioxane yielded 13.4 g (64%) of **16**·HI, identical (mp, ir) to the one prepared by the preceding procedure.

Attempts at Preparing **8d** and **e** Respectively from Methylthiopyrimidine **16**.

A solution of 5.2 g (0.015 mole) of **16**·HI and 1.4 g (0.015 mole) of aniline in 40 ml of propanol was heated at reflux for 17 hours. The solvent was removed *in vacuo* yielding a resinous residue, which (according to tlc) consists of ten products. No solid base and no pure picrate could be separated from the mixture. Similarly, heating of equimolar amounts of **16**·HI and aniline without solvent for 17 hours at 100° yielded a mixture of numerous reaction products none of which could be separated. Boiling of equimolar amounts of **16**·HI and of *p*-methoxyaniline in propanol or heating without solvent in analogy to the preceding experiments also yielded mixtures of many reaction products, none of which could be isolated.

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[14] The course of the reactions of guanidine, guanidinecarbonate and benzylguanidine respectively with 4-phenyl-3-buten-2-one under varying conditions (O_2; N_2; high and low temperature; different solvents) is under further investigation.

[15] Some peculiarities in the nmr spectra of **9d** and **12** (atypical chemical shifts of *o*- and *p*-phenyl protons) will be discussed separately.

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