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HETEROCYCLIC ANALOGS OF PLEIADIENE. 67.* FORMYLATION OF PERIMIDONES, 2,3-DIHYDROPERIMIDINES, AND PERIMIDINES

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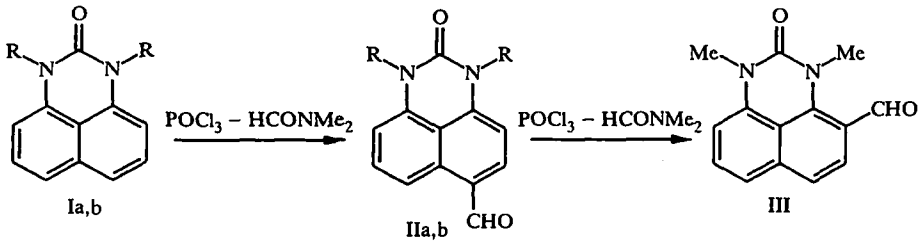
Vilsmeier formylation of 1,3-dialkylperimidones, 1,3-dialkyl-2,3-dihydroperimidines, and 2-trifluoromethylperimidines is performed. The ^{1}H NMR spectra of the resulting mono- and dialdehydes are discussed.

Perimidones, 2,3-dihydroperimidines [2, 3] and perimidines [4] are known to be easily acylated at the 6(7)-(*para*) or 4(9)-(*ortho*) positions. Carboxylic acids in polyphosphoric acid were used as the acylating agents. For perimidones, acyl chlorides in the presence of anhydrous $AlCl_3$ were used [5]. Therefore, we expected that formylation of these compounds might proceed just as easily. The present work tests that hypothesis.

We found that 1,3-dialkylperimidones (Ia and Ib) undergo the Vilsmeier reaction ($POCl_3$–DMF) at 60-80°C to form the perimidon-6-carboxaldehydes IIa, b in 80-85% yield. It seemed interesting to determine if the monoaldehydes could be further formylated, keeping in mind that perimidones readily undergo diacylation [3]. Heating IIa with an excess of Vilsmeier reagent (60-80°C, 5.5 h) led to formation of resin. The only product in about 20% yield was 1,3-dimethylperimidon-4-carboxaldehyde (III), which was somewhat unexpectedly isolated. A similar isomerization was previously observed for 6-acylperimidines with an unsubstituted N–H group [4]. It was proposed that this isomerization is driven by the formation in 9-acyl derivatives of a strong intramolecular hydrogen bond (IHB). Since this is not a factor for aldehyde III, the migration of the formyl group to the more sterically hindered *ortho* position is apparently due to some other reason. It is noteworthy that aldehyde IIa is completely destroyed by heating with polyphosphoric acid for ~30 min, forming a dark green crystalline product. Judging from the PMR spectrum, the product is a complex mixture of oligomers. The tendency to oligomerize in acidic medium probably explains the relatively low yield of III.



a R = Me, b R = Et

Formylation of 1,3-dimethyl-2,3-dihydroperimidine (IV) is more complicated and significantly less regioselective. The reaction goes slowly even at -20-(-30)°C. However, it is better conducted at room temperature.

* For No. 66, see [1].

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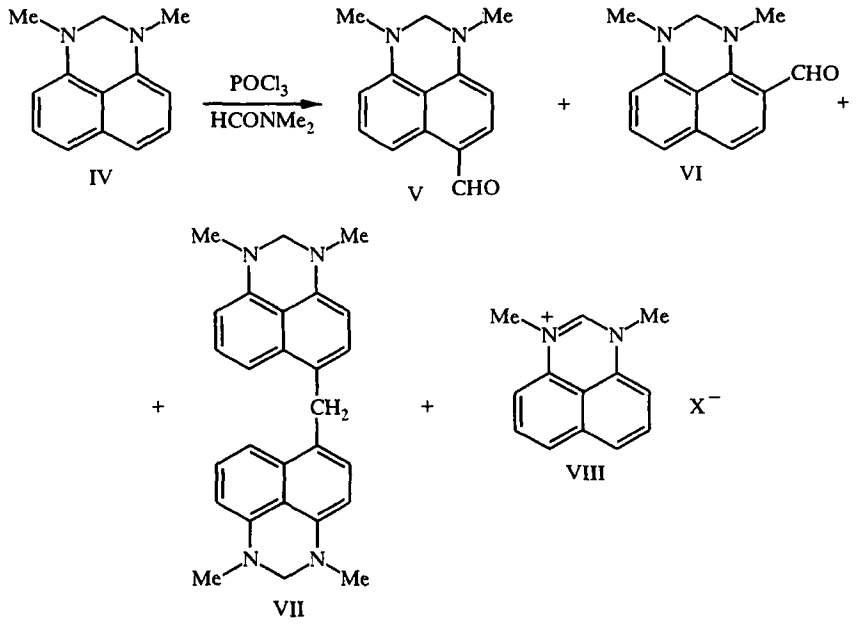
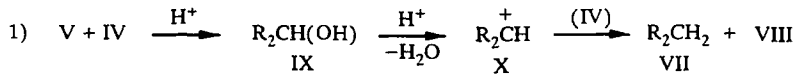
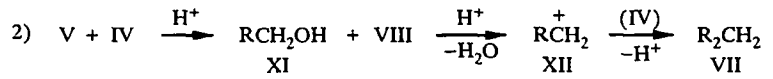
The principal products are the 6-formyl (V) and 4-formyl (VI) derivatives in addition to bis(1,3-dimethyl-2,3-dihydroperimidin-6-yl)methane (VII), the yields of which are 18, 5.5 and 19%, respectively. Furthermore, the 1,3-dimethylperimidinium salt (VIII) was isolated from the reaction mixture (as perchlorate) in 16% yield. (The yields were based on quantitative analysis of the crude product using ^{1}H NMR. The data obtained agreed closely with the results from chromatographic separation of the compounds.)



The formation of VII was highly unexpected. The structure was confirmed by spectral data, including mass spectra. The reaction may proceed by one of the two following schemes:



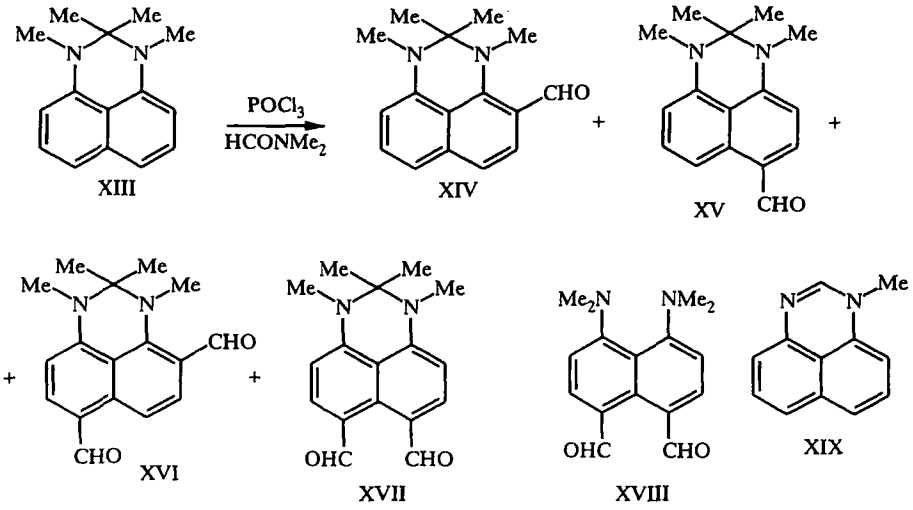


R = 1,3-dimethyl-2,3-dihydroperimidinyl-6

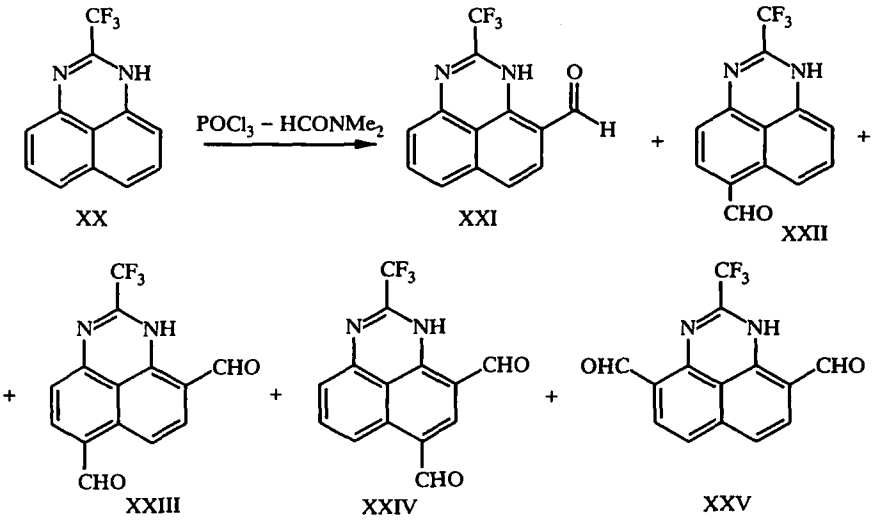
According to the first scheme, IV, which is highly nucleophilic, adds to the carbonyl group of the 6-aldehyde under the acid-catalysis conditions. The secondary alcohol IX formed by this generates a resonance-stabilized carbonium ion X, which accepts a hydride ion from the CH_2 group of the starting material IV. As a result, the diperimidinylmethane VII and the perimidinium cation VIII are formed. According to the second scheme, aldehyde V is reduced in the first step by dihydroperimidine, forming the primary alcohol XI, which then follows a similar path to VII. We prefer the latter scheme since it was confirmed by experiment. (These data will be reported in one of the following articles.) Furthermore, if the reaction were to occur by the first scheme, the formation of a secondary alcohol of type IX would be evident during formylation of 1,2,2,3-tetramethyl-2,3-dihydroperimidine (XIII), which is more nucleophilic than IV but cannot donate a hydride. However, this is not observed.

A small excess of Vilsmeier reagent reacts with XIII at room temperature to give the 4- (XIV) and 6- (XV) aldehydes and the 4,7- (XVI) and 6,7- (XVII) diformyl derivatives in yields of 3, 31, 6 and 7%, respectively. The peridialdehyde XVII is especially interesting because it is stable to storage in air and heating. It is well known that naphthalene-1,8-dialdehyde as such can be obtained only under special conditions [6] because it forms a cyclic monohydrate in air. The stability of dialdehyde XVII, in analogy with other stable perialdehydes, e.g.,

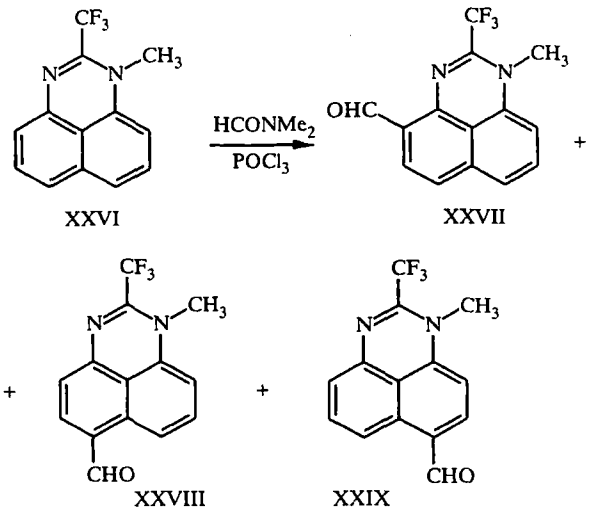
4,5-diformyl-1,8-bis(dimethylamino)naphthalene (XVIII) [7], may be explained by the strong electron-donating effect of the dimethylamino groups, which reduce the positive charge on the carbon atoms of the carbonyls. As a result, nucleophilic addition of water to them is hindered. A noteworthy feature of XVII is that it does not undergo an intramolecular Cannizzaro reaction in boiling in water to form naphtha[1,8-*c*,*d*]pyranone, in contrast with XVIII [7]. This is probably due to both the lower tendency of XVII to hydratation and the substantially reduced basicity, which does not provide the necessary basicity of the medium.



We were unable to formylate 1-methylperimidine (XIX) even with prolonged heating at 90-100°C although characteristic signs of the reaction (deep reddening of the mixture) were observed. Perhaps the obviously lowered reactivity of XIX is due to the relatively high basicity of the perimidines. Thus, the pK_a of XIX in acetonitrile is 13.70 [8], which is much greater than that of IV and VIII (pK_a values of 8.67 and 10.51, respectively) [9] and even more so of the perimidones ($pK_a < 5$) [9]. As a result, XIX under the reaction conditions apparently produces the perimidinium salt, which is inert toward the Vilsmeier reagent. This hypothesis was confirmed by the successful formylation of slightly basic 2-trifluoromethylperimidine (XX) (the pK_a value of its N-methyl derivative XXVI is 6.64) [10]. The principal product (42% yield) was the 9-aldehyde XXI, which is stabilized by an IHB (δ_{NH} = 12.32 ppm). Moreover, the 6-aldehyde XXII (22%) and small quantities of dialdehydes XXIII-XXV were isolated from the reaction mixture. Only the 4,9-dialdehyde (XXV) could be obtained pure. Dialdehydes XXIII and XXIV were not separated owing to their identical chromatographic mobility on Al_2O_3 and silica gel. However, assignment of the signals in the ^1H NMR of this mixture to one isomer or the other is simple (see below).



In analogy with XX, we also formylated 1-methyl-2-trifluoromethylperimidine (XXVI). The products were the 4-formyl (XXVII), 6-formyl (XXVIII) and 7-formyl (XXIX) derivatives in the ratio 22:20:58. Thus, the benzene ring in XXVI that is bound to the pyrrole nitrogen atom is much more reactive than that bound to the pyridine nitrogen atom.



XXVI XXVII XXVIII XXIX

It is noteworthy that it is much more difficult to formylate XXVI than XX, which has a free NH group. Thus, the reaction of XXVI is noticeable only at 80°C. The total yield of XXVII-XXIX after 3.5 h is 46% with 36% of the starting material left unreacted. For XX, the formylation is already complete after 2.5 h at 35°C. It can be assumed that the NH group in XX is involved, e.g., through an IHB, in the stabilization of the intermediate responsible for *ortho* formylation. Considering the high acidity of the NH in XX, it could also be that formylation even in a medium made so acidic by the Vilsmeier reagent goes through equilibrium amounts of the N-anion, which is impossible for the N-methyl derivative XXVI.

The structures of the aldehydes produced were confirmed by measuring their ^{1}H NMR spectra. There are several important differences between the spectra of the *para-* and *ortho*-formylperimidines. The first is that a 6-formyl group strongly deshields the neighboring *peri* hydrogen atom, the signal of which shifts to 8.7-8.9 ppm. The corresponding deshielding of the *ortho* hydrogen atom by a 4-formyl group is much less (δ ~7.8 ppm). The carbonyl oxygen in the aldehyde of XXI forms an IHB and therefore cannot substantially exert an anisotropic effect on the *ortho* hydrogen atom, the signal of which occurs at δ 7.38 ppm. The second difference addresses the position of the proton signals from the CHO groups themselves. Whereas the signal of the formyl proton in the 6-aldehydes lies at δ ~10.0 ppm, it is noticeably shifted to weak field in the 4-aldehydes, from 10.3 ppm in III to 10.75 ppm in XXVII. Apparently this is due to a slightly greater twist angle of the CHO group in the 4-aldehydes relative to the ring system, because of which the diamagnetic component of the ring current has a greater effect on the formyl proton. The fact that the CHO proton signal in XXI, for which the IHB should hold the formyl group in the plane of the ring, occurs at 9.83 ppm argues in favor of this explanation. Finally, the third difference, which again does not extend to XXI, is that the proton signal of a 4-formyl group is usually split into a doublet with a spin–spin coupling constant (SSCC) ^5J ~ 0.8 Hz owing to long-range interaction with H-6 (and not with H-5, which is situated closer). All these differences enable the position of the formyl group in the aldehydes prepared to be easily defined and the signals of the CHO groups in the dialdehydes to be unambigously assigned.

Interesting features of annular tautomerism in the formyl derivatives of 2-trifluoromethylperimidine were found using ^{1}H NMR spectra. As it turned out, two sets of signals are seen in the PMR spectrum of XXII in $CDCl_3$. These correspond to the 6-formyl and 7-formyl tautomers and are caused by NH proton exchange between the two nitrogen atoms and solvent that is slow on the NMR time scale. Also, only one set of signals is observed in DMSO-d_6, which we tentatively assigned to the $N_{(1)}$-H,6-CHO form of XXII. (A more precise identification of the preferred tautomer in DMSO requires additional investigation.) The PMR spectra in $CDCl_3$ of all aldehydes with an *ortho*-formyl group (XXI, XXIII, XXIV and XXV) exhibit a broad NH signal at weak field with δ 12-13 ppm.

This is consistent with the formation of an IHB between the NH and CHO groups. For the monoaldehyde XXI, the bond is preserved even in DMSO-d_6. DMSO breaks the IHB in the dialdehydes. This is especially evident for the 4,9-dialdehyde (XXV). In $CDCl_3$, the molecule is asymmetric, as attested to by the presence in the PMR spectrum of proton signals for two nonequivalent aldehydes and four nonequivalent aromatic protons. In DMSO-d_6, the NH signal at 12.3 ppm disappears, the CHO protons give one signal, and the aromatic protons appear as two two-proton doublets. This suggests that the molecule XXV is symmetric owing to rapid exchange of the NH proton between the nitrogen atom and solvent. The tautomerism of the formyl derivatives of 2-trifluoromethylperimidine will be discussed in more detail in the following report.

EXPERIMENTAL

^1H NMR spectra were recorded on a Unity-300 (300 MHz) instrument with TMS internal standard. UV spectra were obtained on a Specord M40 spectrophotometer. IR spectra were taken from a UR-20 spectrometer. Mass spectra were obtained on a MX-1321A instrument from a direct probe at an ionization chamber temperature 50-100°C and 70 eV ionizing potential. Chromatography was performed on Brockman III activated Al_2O_3 and on Chemapol L40/100 silica gel. Melting points were determined in sealed glass capillaries on a PTP instrument and are uncorrected.

1,3-Dimethylperimidon-6-carboxaldehyde (IIa). Freshly distilled $POCl_3$ (7.5 ml, 0.082 mol) is added dropwise with stirring to purified DMF (20 ml) cooled to 0-(-5)°C. The mixture is stirred at the same temperature for another 30 min. Solution of 1,3-dimethylperimidone (3.18 g, 0.015 mol) in DMF (120 ml) is added to the Vilsmeier reagent over 10-15 min. The resulting red suspension is stirred for 2 h 30 min at 80-90°C and then cooled to room temperature. Water (700 ml) is added, producing a voluminous orange precipitate. The suspension is adjusted to pH 9 with 20% KOH. The precipitate is filtered off, washed with water and dried in air. The crude aldehyde is dissolved in $CHCl_3$ (~100 ml) and passed over an Al_2O_3 column (l = 30 cm, d = 4 cm) in order to purify it from a small amount of resin and a small quantity (~0.04 g, R_f 0.2 in $CHCl_3$) of red impurity of undefined structure. The first fraction eluted by $CHCl_3$ (R_f 0.36) is collected. Yield 2.5 g (69%). Aldehyde IIa is obtained as bright yellow crystals with mp 241-242°C after recrystallization from ethanol. PMR spectrum ($CDCl_3$): 3.47 (3H, s, 1-CH_3), 3.50 (3H, s, 3-CH_3), 6.63 (1H, d, J_{45} = 8.20 Hz, 4-H), 6.76 (1H, dd, J_{98} = 7.84, J_{97} = 0.66 Hz, 9-H), 7.60 (1H, dd, J_{87} = 8.57, J_{89} = 7.84 Hz, 8-H), 7.83 (1H, d, J_{54} = 8.20 Hz, 5-H), 8.83 (1H, dd, J_{78} = 8.57, J_{79} = 0.87 Hz, 7-H), 10.07 ppm (1H, s, CHO). IR spectrum (vaseline oil): 1679 (both C=O groups), 1620, 1595 cm^{-1} (ring). UV spectrum (methanol), λ_{max} (log ε): 240, sh (4.20), 263 (4.27), 326 sh (3.79), 342 (3.86), 385 nm (4.14). Found, %: C 69.70; H 5.05; N 11.42. $C_{14}H_{12}N_2O_2$. Calculated, %: C 69.97; H 5.04; N 11.66.

1,3-Diethylperimidon-6-carboxaldehyde (IIb) is prepared analogously to compound IIa from 1,3-diethylperimidone. Yield after purification by chromatography (R_f 0.74), 60%. Yellow crystals with mp 185-186°C (ethanol). PMR spectrum ($CDCl_3$): 1.35 (6H, m, $2CH_2C\underline{H}_3$), 4.12 (4H, m, $2C\underline{H}_2CH_3$), 6.70 (1H, d, J_{45} = 8.22 Hz, 4-H), 6.82 (1H, dd, J_{98} = 7.60, J_{97} < 1 Hz, 9-H), 7.59 (1H, dd, J_{87} = 8.58, J_{89} = 7.60 Hz, 8-H), 7.83 (1H, d, J_{54} = 8.18 Hz, 5-H), 8.83 (1H, dd, J_{78} = 8.58, J_{79} < 1 Hz, 7-H), 10.08 ppm (1H, s, CHO). IR spectrum (vaseline oil): 1695 (both C=O groups), 1635, 1595 cm^{-1} (ring). Found, %: C 71.50; H 6.32; N 10.13. $C_{16}H_{16}N_2O_2$. Calculated, %: C 71.61; H 6.01; N 10.45.

1,3-Dimethylperimidon-4-carboxaldehyde (III). Solution of IIa (0.08 g, 0.3 mmol) in DMF (4 ml) is added in portions to Vilsmeier reagent prepared from $POCl_3$ (0.2 ml, 2 mmol) and DMF (2.5 ml). The mixture, which rapidly changes color from light yellow to brown, is stirred for 5 h 30 min at 60-80°C. Water (10 ml) is added. The pH is adjusted to 9 with 20% KOH. The finely crystalline precipitate is filtered using a fluted filter (precipitate 1). The filtrate is extracted with $CHCl_3$ (10 ml). The extract is evaporated and dried in air (precipitate 2). Precipitates 1 and 2 are combined, treated with heating with $CHCl_3$ and filtered. The insoluble solids are discarded. The filtrate is passed over an Al_2O_3 column (l = 22 cm, d = 2 cm). The first yellow fraction, which contains a small quantity of impurities, eluted by $CHCl_3$–hexane (2:1) is collected. Yield 0.025 g of III with a small amount of red impurity, which is removed using preparative thin-layer chromatography on Al_2O_3 (eluent $CHCl_3$). Yield of pure III 0.015 g (19%). Lemon-yellow crystals; mp 165-166°C (ethyl acetate). PMR spectrum

($CDCl_3$): 3.52 (3H, s, 1-CH_3), 3.63 (3H, s, 3-CH_3), 6.77 (1H, dd, J_{98} = 7.76, J_{97} < 1 Hz, 9-H), 7.36 (1H, d, J_{65} = 8.71 Hz, 6-H), 7.37 (1H, dd, J_{78} = 8.17, J_{79} < 1 Hz, 7-H), 7.56 (1H, dd, J_{87} = 8.13, J_{89} = 7.76 Hz, 8-H), 7.82 (1H, d, J_{56} = 8.71 Hz, 5-H), 10.26 ppm (1H, s, CHO). IR spectrum (vaseline oil): 1680 (both C=O groups), 1620, 1575 cm^{-1} (ring). Found, %: C 70.31; H 5.50; N 11.26. $C_{14}H_{12}N_2O_2$. Calculated, %: C 69.97; H 5.04; N 11.66.

Formylation of 1,3-Dimethyl-2,3-dihydroperimidine (IV). Vilsmeier reagent prepared from $POCl_3$ (0.45 ml, 4 mmol) and DMF (1.5 ml) is added dropwise over 20 min to solution of IV (0.8 g, 4 mmol) in mixture of dry DMF (15 ml) and toluene (8 ml) cooled to -13°C. The red reaction mixture is stirred for 1 h 45 min at -15°C. Water (40 ml) is added. Toluene (15 ml) is added to the orange solution. The mixture is shaken. The layers separate. Yellow crystals (fraction 1) are isolated from the toluene layer before the solvent is distilled. The aqueous layer is neutralized with 20% KOH until the pH is 7 and is then extracted with toluene (20 ml). Yellowish crystals (0.14 g, fraction 2) are obtained after the solvent is evaporated.

Fraction 1 is dissolved in the minimal amount of $CHCl_3$ and passed over an Al_2O_3 column (l = 15 cm, d = 3 cm) with $CHCl_3$ eluent. The starting material (0.08 g, 10%) elutes first. A yellow fraction containing the 6- and 4-aldehydes together with a small amount of VII is then collected. After the solvent is distilled, the solid is dissolved in a small amount of conc. HCl. Water is added to precipitate the practically pure 6-aldehyde V. Yield 0.16 g (~18%). Treating the filtrate with conc. NH_4OH until the pH is 2-3 precipitates a mixture of the 4-aldehyde VI and VII. These are separated using preparative thin-layer chromatography on silica gel with $CHCl_3$ eluent. Yield 0.05 g (5.5%) of the 4-aldehyde and 0.01 g of VII.

Fraction 2 is practically pure di(1,3-dimethyl-2,3-dihydroperimidin-6-yl)methane (VII). Total yield 0.15 g (19%).

Adding an excess of dry sodium perchlorate and partially evaporating the water from the neutralized aqueous layer remaining after the isolation of fractions 1 and 2 produces 1,3-dimethylperimidinium perchlorate (VIII, 0.17g, 16%), mp 222°C, which agrees with the literature [11]. PMR spectrum (DMSO-d_6): 3.58 (6H, s, 1- and 3-CH_3), 7.02 (2H, dd, J_{45} = J_{98} = 7.45, J_{46} = J_{97} = 0.41 Hz, 4- and 9-H), 7.59 (2H, dd, J_{54} = J_{89} = 7.45, J_{56} = J_{87} = 7.85 Hz, 5- and 8-H), 7.70 (2H, dd, J_{65} = J_{78} = 7.85 Hz, J_{64} = J_{79} = 0.41 Hz, 6- and 7-H), 9.00 ppm (1H, s, 2-H).

1,3-Dimethyl-2,3-dihydroperimidin-6-carboxaldehyde (V). Yellow crystals with mp 116-118°C are readily soluble in the majority of organic solvents and poorly soluble in alkanes. The compound decomposes in solution with heating or prolonged standing at room temperature. A satisfactory solvent for its recrystallization could not be found. PMR spectrum ($CDCl_3$): 2.99 (3H, s, 1-CH_3), 3.12 (3H, s, 3-CH_3), 4.29 (2H, s, CH_2), 6.51 (1H, d, J_{45} = 8.20 Hz, 4-H), 6.63 (1H, dd, J_{98} = 7.77, J_{97} = 0.76 Hz, 9-H), 7.53 (1H, dd, J_{87} = 8.53, J_{89} = 7.77 Hz, 8-H), 7.79 (1H, d, J_{54} = 8.20 Hz, 5-H), 8.74 (1H, dd, J_{78} = 8.53, J_{79} = 0.76 Hz, 7-H), 10.05 ppm (1H, s, CHO). IR spectrum ($CHCl_3$): 1660 (C=O), 1585 cm^{-1} (ring). Found, %: C 74.71; H 6.47; N 12.11. $C_{14}H_{14}N_2O$. Calculated, %: C 74.30; H 6.24; N 12.39.

1,3-Dimethyl-2,3-dihydroperimidin-4-carboxaldehyde (VI). Yellow caramel. The compound could not be prepared sufficiently pure because of its tendency to decompose on heating in solution. PMR spectrum ($CDCl_3$): 3.02 (3H, s, 1-CH_3), 3.05 (3H, s, 3-CH_3), 4.20 (2H, s, CH_2), 6.58 (1H, dd, J_{98} = 7.69, J_{97} < 1 Hz, 9-H), 7.18 (1H, dd, J_{78} = 8.02, J_{79} < 1 Hz, 7-H), 7.43 (1H, d, J_{65} = 8.57 Hz, 6-H), 7.45 (1H, dd, J_{87} = 8.02, J_{89} = 7.69 Hz, 8-H), 7.78 (1H, d, J_{56} = 8.57 Hz, 5-H), 10.45 ppm (1H, s, CHO).

Bis(1,3-dimethyl-2,3-dihydroperimidin-6-yl)methane (VII). Slightly yellowish crystals with mp 220-222°C (heptane). PMR spectrum ($CDCl_3$): 2.95 (6H, s, 3- and 3'-CH_3), 3.04 (6H, s, 1- and 1'-CH_3), 4.15 (4H, s, 2- and 2'-CH_2), 6.42 (2H, d, J_{45} = $J_{4'5'}$ = 7.84 Hz, 4- and 4'-H), 6.58 (2H, dd, J_{98} = $J_{9'8'}$ = 7.10, J_{97} = $J_{9'7'}$ = 1.39 Hz, 9- and 9'-H), 6.95 (2H, d, J_{54} = $J_{5'4'}$ = 7.84 Hz, 5- and 5'-H), 7.34 (2H, dd, J_{87} = $J_{8'7'}$ = 8.49, J_{89} = $J_{8'9'}$ = 7.10 Hz, 8- and 8'-H), 7.39 ppm (2H, dd, J_{78} = $J_{7'8'}$ = 8.49, J_{79} = $J_{7'9'}$ = 1.39 Hz, 7- and 7'-H). IR spectrum ($CHCl_3$): 1595 cm^{-1} (vw, ring). Mass spectrum, m/z (I, %): 408 (M^+) (100%), 211 (24), 197 (10), 196 (12), 195 (12), 167 (12), 115 (6). Found, %: C 79.21; H 6.60; N 13.43. $C_{27}H_{28}N_4$. Calculated, %: C 79.38; H 6.91; N 13.71.

Formylation of 1,2,2,3-Tetramethyl-2,3-dihydroperimidine (XIII). Solution of Vilsmeier reagent prepared from $POCl_3$ (0.62 ml, 6.8 mmol) and DMF (2.0 ml) was added in portions dropwise to solution of XIII (0.7 g, 3 mmol) in DMF (20 ml) cooled to -10°C. The reddish-orange mixture was stirred for 30 min at -10-(-5)°C and then for 2 h at room temperature. Water (50 ml) was added. The mixture was neutralized with 20% KOH until pH 9. The yellowish-orange emulsion was extracted with $CHCl_3$ (3×100 ml). The extract was washed with water.

The $CHCl_3$ layer was separated, evaporated to a small volume, and passed over an Al_2O_3 column (l = 15 cm, d = 2 cm) with $CHCl_3$ eluent. Unreacted starting material, the closely eluting fractions of the 4-aldehyde XIV and 6-aldehyde XV, and the 4,7-aldehyde XVI are eluted from the column without separation. The *peri* dialdehyde XVII remains at the top. The top portion is isolated and XVII is extracted with $CHCl_3$ in a Soxhlet extractor.

Preparative thin-layer chromatography on III-grade activated Al_2O_3 (eluent $CHCl_3$–hexane, 1:1) is used to isolate starting material (0.1 g, 14%, R_f 0.9) and aldehydes XIV, XV and XVI from the eluate.

1,2,2,3-Tetramethyl-2,3-dihydroperimidin-4-carboxaldehyde (XIV). Yield 0.025 g (3%). Bright yellow caramel with R_f 0.5. PMR spectrum ($CDCl_3$): 1.47 (6H, s, 2-CH_3×2), 2.77 (3H, s, 1-CH_3), 2.98 (3H, s, 3-CH_3), 6.60 (1H, d, J_{98} = 7.91 Hz, 9-H), 7.15 (1H, d, J_{78} = 7.99 Hz, 7-H), 7.44 (1H, dd, J_{65} = 8.57, $J_{6\text{-CHO}}$ = 0.88 Hz, 6-H), 7.47 (1H, dd, J_{87} = 7.99, J_{89} = 7.91 Hz, 8-H), 7.80 (1H, d, J_{56} = 8.65 Hz, 5-H), 10.50 ppm (1H, d, $J_{\text{CHO-6}}$ = 0.88 Hz, 4-CHO). IR spectrum ($CHCl_3$): 1670 (C=O), 1618, 1582 cm^{-1} (ring). UV spectrum (methanol), λ_{max} (log ε): 235, sh (4.04), 239 (4.36), 344 nm (3.93). Found, %: C 75.64; H 7.25; N 10.86. $C_{16}H_{18}N_2O$. Calculated, %: C 75.56; H 7.13; N 11.01.

1,2,2,3-Tetramethyl-2,3-dihydroperimidin-6-carboxaldehyde (XV). Yield 0.26 g (31%). R_f 0.35. Yellow crystals with mp 127-128°C (*n*-octane). PMR spectrum ($CDCl_3$): 1.45 (6H, s, 2-CH_3×2), 2.92 (3H, s, 1-CH_3), 3.08 (3H, s, 3-CH_3), 6.53 (1H, d, J_{45} = 8.35 Hz, 4-H), 6.72 (1H, d, J_{98} = 7.91 Hz, 9-H), 7.52 (1H, dd, J_{87} = J_{89} = 7.91 Hz, 8-H), 7.77 (1H, d, J_{54} = 8.35 Hz, 5-H), 8.74 (1H, d, J_{78} = 7.91 Hz, 7-H), 10.01 ppm (1H, s, CHO). IR spectrum (vaseline oil): 1660 (C=O), 1590 cm^{-1} (ring). UV spectrum (methanol), λ_{max} (log ε): 243, sh (4.21), 260 (4.34), 341 (4.12), 400 nm (4.22). Found, %: C 75.48; H 7.22; N 10.92. $C_{16}H_{18}N_2O$. Calculated, %: C 75.56; H 7.13; N 11.01.

1,2,2,3-Tetramethyl-2,3-dihydroperimidin-4,7-dicarboxaldehyde (XVI). Yield 0.05 g (6%). R_f 0.13. Orangish-yellow crystals with mp 134-135°C (*n*-octane). PMR spectrum ($CDCl_3$): 1.49 (6H, s, 2-CH_3×2), 2.74 (3H, s, 1-CH_3), 3.13 (3H, s, 3-CH_3), 6.65 (1H, d, J_{98} = 8.49 Hz, 9-H), 7.91 (1H, d, J_{89} = 8.49 Hz, 8-H), 8.01 (1H, d, J_{56} = 8.79 Hz, 5-H), 9.01 (1H, dd, J_{65} = 8.79 Hz, $^5J_{6\text{-H-4-CHO}}$ = 0.88 Hz, 6-H), 10.05 (1H, s, 7-CHO), 10.51 ppm (1H, d, $^5J_{\text{CHO-6-H}}$ = 0.88 Hz, 4-CHO). IR spectrum (vaseline oil): 1675 (C=O), 1610, 1605, 1580 cm^{-1} (ring). Found, %: C 72.00; H 6.66; N 9.62. $C_{17}H_{18}N_2O_2$. Calculated, %: C 72.31; H 6.43; N 9.93.

1,2,2,3-Tetramethyl-2,3-dihydroperimidin-6,7-dicarboxaldehyde (XVII). Yield 0.06 g (7%). Brownish needles with mp 190-191°C (toluene). PMR spectrum ($CDCl_3$): 1.52 (6H, s, 2-CH_3×2), 3.10 (6H, s, 1- and 3-CH_3), 6.62 (2H, d, J_{45} = J_{98} = 8.42 Hz, 4- and 9-H), 8.05 (2H, d, J_{54} = J_{89} = 8.42 Hz, 5- and 8-H), 9.92 ppm (2H, s, 6- and 7-CHO). IR spectrum (vaseline oil): 1700, 1673 (C=O), 1580 cm^{-1} (ring). Found, %: C 72.03; H 6.60; N 9.81. $C_{17}H_{18}N_2O_2$. Calculated, %: C 72.31; H 6.43; N 9.93.

Formylation of 2-Trifluoromethylperimidine. Vilsmeier reagent prepared by the standard method from $POCl_3$ (3.7 ml, 0.04 mol) and DMF (10 ml) was added dropwise to solution of 2-trifluoromethylperimidine (XX, 4.4 g, 0.019 mol) in dry DMF (80 ml) cooled to 0°C. The mixture, which gradually acquired a purple color, was stirred for 3 h at 30-35°C. Water (1 l) was added. The orangish-yellow crystals, which are a mixture of the mono- and dialdehydes with traces of the starting material, are filtered off, washed with water and dried in air. Yield 4.5 g (precipitate 1). The filtrate is extracted with $CHCl_3$ (4×100 ml). Additional yield 0.3 g of orange crystals (precipitate 2) containing mainly the 6-aldehyde XXII and the 4,9-dialdehyde XXV.

Precipitate 1 is dissolved in the minimal amount of $CHCl_3$ and passed over an Al_2O_3 column (l = 25 cm, d = 2 cm) with $CHCl_3$ eluent. Practically pure 9-aldehyde XXI elutes from the column whereas the remaining formylation products are poorly mobile. These are extracted from the column material in a Soxhlet extractor by $CHCl_3$. The solid from evaporating the $CHCl_3$ is combined with precipitate 2. Fractional crystallization from *n*-octane isolates most of the 6-aldehyde XXII, which separates first from hot octane and is removed. A mixture of dialdehydes XXIII-XXV precipitates from the warm mother liquor. A small quantity of starting material remains in solution.

The more mobile 4,9-dialdehyde XXV is easily separated from the mixture of dialdehydes using preparative thin-layer chromatography on Al_2O_3 ($CHCl_3$–EtOH eluent, 2:1). The mixture of the less mobile 6,9- (XXIII) and 7,9-dialdehyde XXIV, which are present in a 3:5 ratio according to PMR data, could not be separated. Total yield 0.25 g (4.6%).

2-Trifluoromethylperimidin-9-carboxaldehyde (XXI). Yield 2.05 g (42%). Yellow crystals with mp 160-162°C (*n*-octane). R_f 0.70. PMR spectrum ($CDCl_3$): 7.17 (1H, d, J_{78} = 8.81 Hz, 7-H), 7.27 (1H, dd, J_{45} = 7.20, J_{46} < 1 Hz, 4-H), 7.38 (1H, d, J_{87} = 8.81 Hz, 8-H), 7.42 (1H, dd, J_{65} = 8.00, J_{64} < 1 Hz, 6-H), 7.62 (1H, dd, J_{54} = 7.20, J_{56} = 8.00 Hz, 5-H), 9.83 (1H, s, CHO), 12.32 ppm (1H, br. s, NH). IR spectrum (vaseline oil): 1633 (C=O), 1620, 1580 cm^{-1} (ring). UV spectrum (methanol), λ_{max} (log ε): 238, sh (3.91), 264 (4.55), 316, sh (3.41), 329 (3.86), 412 nm (4.07). Found, %: C 58.79; H 2.50; N 10.32. $C_{13}H_7F_3N_2O$. Calculated, %: C 59.10; H 2.67; N 10.60.

2-Trifluoromethylperimidin-6-carboxaldehyde (XXII). Yield 0.95 g (19%). Bright orange crystals with mp 212-214°C (dec.) (octane). R_f 0.02. The compound noticeably decomposes upon attempted purification using Al_2O_3 column chromatography. PMR spectrum (DMSO-d_6): 6.75 (1H, d, J_{45} = 8.02 Hz, 4-H), 7.03 (1H, br. dd, J_{98} = 7.36, J_{97} << 1 Hz, 9-H), 7.55 (1H, dd, J_{87} = 8.46, J_{89} = 7.36 Hz, 8-H), 7.85 (1H, d, J_{54} = 8.02 Hz, 5-H), 8.64 (1H, dd, J_{78} = 8.46, J_{79} << 1 Hz, 7-H), 9.89 ppm (1H, s, CHO). IR spectrum (vaseline oil): 3450-3050 (br. band of medium intensity with fine structure, NH), 1647 (C=O), 1620, 1590, 1567, 1527 cm^{-1} (ring). Found, %: C 58.97; H 2.66; N 10.48. $C_{13}H_7F_3N_2O$. Calculated, %: C 59.10; H 2.67; N 10.60.

2-Trifluoromethylperimidin-6,9-dicarboxaldehyde (XXIII). PMR spectrum ($CDCl_3$): 7.40 (1H, d, J_{45} = 8.06 Hz, 4-H), 7.78 (1H, d, J_{87} = 9.04 Hz, 8-H), 8.12 (1H, d, J_{54} = 8.06 Hz, 5-H), 8.84 (1H, d, J_{78} = 9.04 Hz, 7-H), 9.99 (1H, s, 9-CHO), 10.18 (1H, s, 6-CHO), 12.77 ppm (1H, br. s, NH).

2-Trifluoromethylperimidin-7,9-dicarboxaldehyde (XXIV). Isolated in a mixture with XXIII. PMR spectrum ($CDCl_3$): 7.61 (1H, dd, J_{45} = 7.82, J_{46} = 0.76 Hz, 4-H), 7.96 (1H, dd, J_{56} = 8.44, J_{54} = 7.82 Hz, 5-H), 8.00 (1H, s, 8-H), 9.10 (1H, dd, J_{65} = 8.44, J_{64} = 0.76 Hz, 6-H), 9.96 (1H, s, 9-CHO), 10.40 (1H, s, 7-CHO), 13.00 ppm (1H, br. s, NH).

2-Trifluoromethyl-4,9-dicarboxaldehyde (XXV). Yield 0.15 g (2.8%). Light brown crystals with mp 211-214°C (ethanol). R_f 0.3. PMR spectrum ($CDCl_3$): 7.31 (1H, d, J_{78} = 8.67 Hz, 7-H), 7.44 (1H, dd, J_{65} = 8.68, $J_{6\text{-H}\text{-}4\text{-CHO}}$ = 0.40 Hz, 6-H), 7.65 (1H, d, J_{87} = 8.67 Hz, 8-H), 8.08 (1H, d, J_{56} = 8.68 Hz, 5-H), 9.93 (1H, s, 9-CHO), 10.83 (1H, d, $J_{4\text{-CHO}\text{-}6\text{-H}}$ = 0.40 Hz, 4-CHO), 12.69 ppm (1H, br. s, NH); (DMSO-d_6, 100°C): 7.40 (2H, d, 6,7-H, J_{65} = J_{78} = 8.72 Hz), 7.85 (2H, d, 5,8-H, J_{56} = J_{87} = 8.72 Hz), 10.38 ppm (2H, s, 4,9-CHO). Found, %: C 57.83; H 2.60; N 9.49. $C_{14}H_7F_3N_2O_2$. Calculated, %: C 57.54; H 2.41; N 9.59.

Formylation of 1-Methyl-2-trifluoromethylperimidine (XXVI). Vilsmeier reagent prepared by the standard method from $POCl_3$ (0.3 ml, 3.3 mmol) and DMF (1.5 ml) is added over 30 min with stirring to solution of XXVI (0.25 g, 1 mmol) in dry DMF (15 ml). The mixture is stirred for 3.5 h at 80°C. The color gradually deepens to dark purple. The reaction mixture is cooled. Water (100 ml) is added. The yellowish-green emulsion is extracted with $CHCl_3$ (150 ml). The extract is evaporated to dryness, producing 0.24 g of viscous solid. Three fractions are isolated by preparative thin-layer chromatography on silica gel ($CHCl_3$ eluent). These are unreacted starting material (R_f 0.3), 0.09 g (36%), the 4-aldehyde (XXVII, R_f 0.2, 0.03 g, 10.5%), and a mixture of the 6- (XXVIII) and 7-aldehyde (XXIX) (R_f 0.1, 1:3 ratio according to ^{1}H NMR data, 0.10 g, 36%).

1-Methyl-2-trifluoromethylperimidin-4-carboxaldehyde (XXVII). Bright yellow crystals with mp 194-196°C (octane). PMR spectrum ($CDCl_3$): 3.40 (3H, q, CH_3, $^5J_{CH_3\text{-}CF_3}$ = 0.93 Hz), 6.56 (1H, d, J_{98} = 7.80, J_{97} << 1 Hz), 7.28 (2H, m, 6- and 7-H), 7.44 (1H, dd, J_{87} = 8.02, J_{89} = 7.80 Hz, 8-H), 7.75 (1H, d, J_{56} = 8.68 Hz, 5-H), 10.75 ppm (1H, d, CHO, $^5J_{CHO\text{-}6\text{-H}}$ = 0.70 Hz). Found, %: C 60.40; H 3.37; N 10.23. $C_{14}H_9F_3N_2O$. Calculated, %: C 60.44; H 3.26; N 10.07.

1-Methyl-2-trifluoromethylperimidin-6-carboxaldehyde (XXVIII). PMR spectrum ($CDCl_3$): 3.42 (3H, s, CH_3), 6.71 (1H, dd, J_{98} = 7.97, J_{97} = 0.70 Hz, 9-H), 7.12 (1H, d, J_{45} = 7.80 Hz, 4-H), 7.57 (1H, dd, J_{87} = 8.70, J_{89} = 7.97 Hz, 8-H), 7.84 (1H, d, J_{54} = 7.80 Hz, 5-H), 8.86 (1H, dd, J_{78} = 8.70, J_{79} = 0.70 Hz, 7-H), 10.08 (1H, s, 6-CHO).

1-Methyl-2-trifluoromethylperimidin-7-carboxaldehyde (XXIX). PMR spectrum ($CDCl_3$): 3.43 (3H, s, CH_3), 6.50 (1H, d, J_{98} = 8.15 Hz, 9-H), 7.32 (1H, dd, J_{45} = 7.55, J_{46} = 0.80 Hz, 4-H), 7.66 (1H, dd, J_{54} = 7.55, J_{56} = 8.56 Hz, 5-H), 7.76 (1H, d, J_{89} = 8.15 Hz, 8-H), 8.95 (1H, dd, J_{65} = 8.56, J_{64} = 0.92 Hz. 6-H), 10.01 (1H, s, 7-CHO).

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