Quantitative Gas-Solid Diazotization of 3-Aminopyrazolo[3,4-*b*]pyridine Derivatives and Azo Dye Syntheses by Means of Solid-Solid Reactions

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Gas-solid and solid-solid techniques allow for waste-free quantitative syntheses and coupling reactions of the heterocyclic diazonium salts **2**. The solid-state diazotization of **1a** with gaseous NO_2 has been mechanistically investigated by atomic force microscopy (AFM). Azo couplings are achieved in quantitative yields by cautious co-grinding of the solid diazonium salt **2a** with five (thio)barbituric acids, six acetoacetanilides (these couplings are followed by internal cyclization in solid-state cascades), β-naphthol, and 2,6-dimethylphenol. The solid diazonium salt **2a** is quantitatively coupled with three solid anilines to give the tautomeric triazenes **16**. The structures of the products were established with IR, NMR and mass spectroscopy, while the tautomeric properties of the compounds were judged by density functional calculations at the B3LYP/6–31G* and BLYP/6–31G** levels.

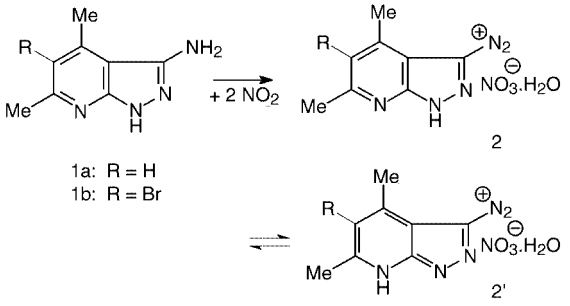
Introduction

Solid diazonium nitrates are quantitatively obtained by the action of gaseous NO_2 on solid anilines.[1,2] These reacted quantitatively in solid-state diazo couplings.[1,2] The considerable biological activity of fused pyrazoles[3–5] and the excellent dyeing properties of pyrazolylazo derivatives[6–8] prompted us to explore the solid-state synthesis of 3-aminopyrazolo[3,4-*b*]pyridine diazonium salts and their solid-state couplings with barbituric acids, acetoacetanilides, β-naphthol, 2,6-dimethylphenol, and anilines. Unlike the corresponding solution reactions, the favorable properties of solid-state reactions were expected to give quantitative yields and thus avoid or minimize wastes and save resources. We report on the realization of these expectations in numerous cases.

Results

Solid-State Diazotizations

The quantitative diazotizations of solid aromatic amines with NO_2 gas are most versatile.[1,2,9] Further applications are the diazotizations of 3-aminopyrazolo[3,4-*b*]pyridine derivatives **1a** and **1b**,[10–12] which quantitatively give the monohydrates of the diazonium nitrates **2a** and **2b** without nitrosation at the NH group of the pyrazole ring (Scheme 1). The solid compounds **2a** and **2b** can safely be handled at room temperature, but they explode upon melting at 133 or 143 °C and for safety reasons they should not be exposed to mechanical shock or ball-milled or ground at sharp edges. Their versatility derives from the easy accessibility of **1** from acetylacetone, hydrazine and cyanacetamide.[10–12] The water of hydration in **2** does not interfere with the solid-state coupling reactions and so was not removed.



Scheme 1. Quantitative gas-solid synthesis of stable diazonium nitrate hydrates **2** by treatment of **1** with gaseous NO_2.

Previous reports discussed only formula **2**.[13] However, 3-diazopyrazolo[3,4-*b*]pyridines **2**[14] should be formulated as equilibrium mixtures with the proton at the pyrazole-*N* (**2**) and at the pyridine-*N* (**2′**). Semiempirical PM3 calculations predict the structure **2a** to be 5 kcal·mol^{-1} less stable than **2a′**. DFT calculations (B3LYP/6−31G*), however, predict **2a** to be more stable than **2a′** by the minute amount of 0.53 kcal·mol^{-1} (the energy difference is more pronounced if the methyl groups are omitted: 2.90 kcal·mol^{-1}).

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The tautomeric preference in the crystal lattice is hard to assess without an X-ray crystal structure determination. The solid diazonium salts **2** are stable and can be stored at room temperature. Their typical diazonium bands in the IR are found at 2207 and 2208 cm^{-1}.

Mechanistic Investigation of Diazotization by AFM (Atomic Force Microscopy)

Gas-solid reactions are still not common practice and have yet to find due coverage in textbooks. It is therefore important to establish the solid-state character of the gas-solid diazotizations of **1** at the nanoscopic level, in particular as no crystal structural data for predictions of the feasibility of the required molecular migrations within the crystal[15] are available in this case. AFM is able to distinguish the three-step solid-state mechanism (phase rebuilding, phase transformation, and disintegration)[15–17] from possible intermediate nanoscopic melting,[17] although this would stop the reaction in most cases.[15–17] Short treatment of **1a** on the main face of its single crystal (laths) with 20% NO_2 in air gave large mountains and deep craters with strong structuring that were stable upon repeated measurements (Figure 1).

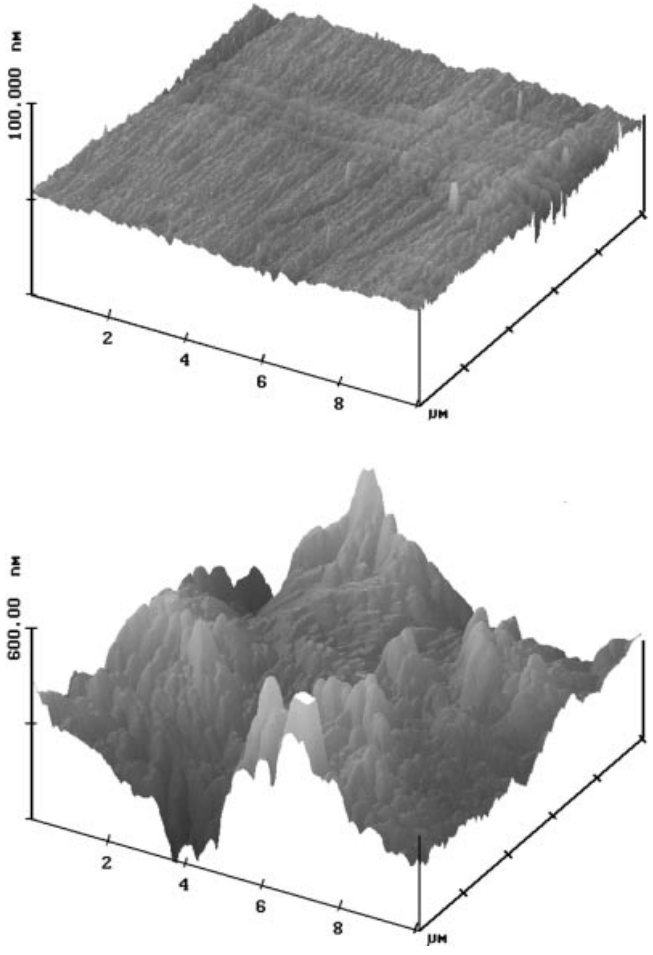


Figure 1. AFM topographies of **1a** (top; the *y* direction is parallel to the long crystal axis) on its main face and (bottom) after application of 5 mL of 20% NO_2 from ca. 1 cm distance for 60 s, showing the result of successful phase transformation into the lattice of **2a**

Evidently, the reaction was so rapid and efficient that we already see the result of the second step, the phase transformation. The phase rebuilding stage (which requires molecular migrations within the original crystal)[15] can only be detected under more moderate conditions (10% NO_2 for 2×15 s) (Figure 2). The initially rather flat surface is immediately changed upon application of the NO_2. The surface features do not align along the surface imperfections but form isolated craters with walls and volcano-like elevations around them (Figure 2, b). These become more uniform upon further reaction (Figure 2, c) and, finally, the phase rebuilding is followed by phase transformation (into the product lattice of **2a**) with the sudden formation of much larger features in Figure 2, d. The lower height of the features than of those in Figure 1 indicates some influence of moisture in the multiple gas applications. The crystal disintegration is thus confirmed by preparative runs in the absence of moisture, when a fine powder is obtained. Clearly, we have favorable crystal packing in **1a**, and this justifies the hope that **2a** may also be reactive in solid-state reactions.

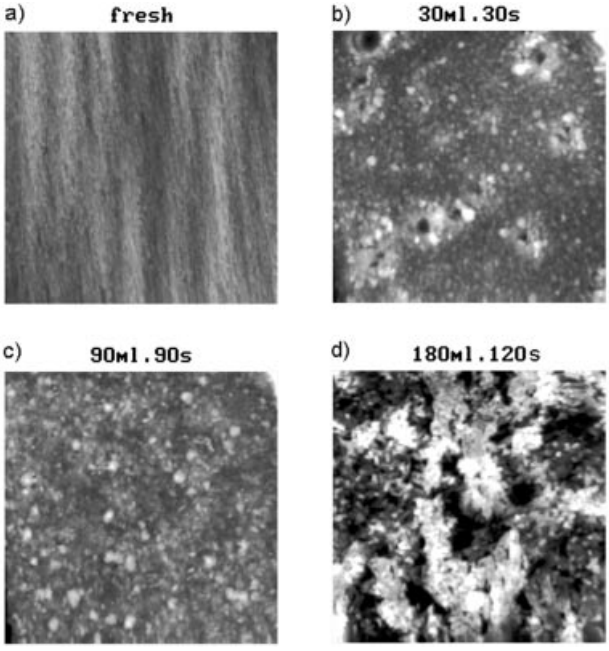
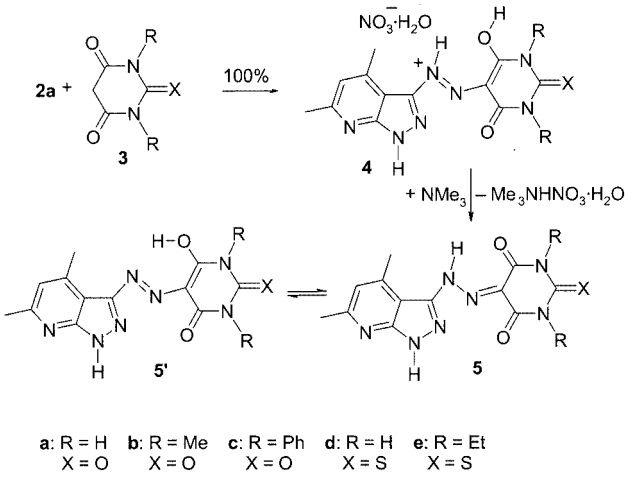


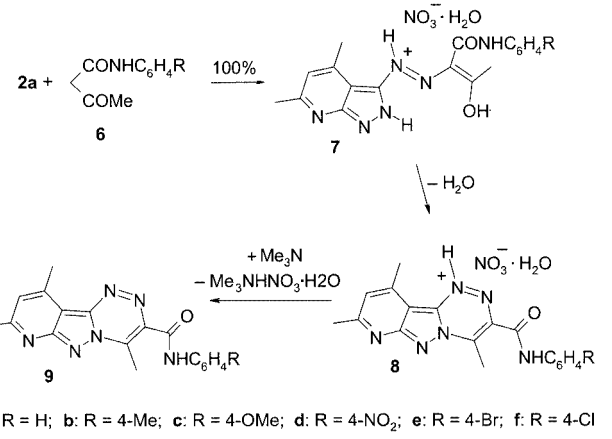
Figure 2. 10 µm AFM topographies on the main surface of **1a**; a) fresh; b), c), d) after application of 10% NO_2 at ca. 1 cm distance in two, four, and six portions from a syringe at the amounts and total interaction times given; the *z* values are 50 nm for a) and 200 nm for b), c), and d)

Solid-State Azo Coupling between 2a and Barbituric Acids, Acetoacetanilides, β-Naphthol, and 2,6-Dimethylphenol

Careful co-grinding of crystalline **2a** with *(thio)barbituric acids* **3a–e** gives quantitative yields of the tautomeric "5-arylazobarbituric acids" **5**. The formation of the salts **4** was waste-free and the free bases **5** were quantitatively obtained by treatment with gaseous trimethylamine and washing with water. The chemical structures of the compounds



Scheme 2. Quantitative solid-state couplings of **2a** with (thio)barbituric acids



Scheme 3. Quantitative solid-state couplings and solid-state in situ cyclizations with acetoacetanilides

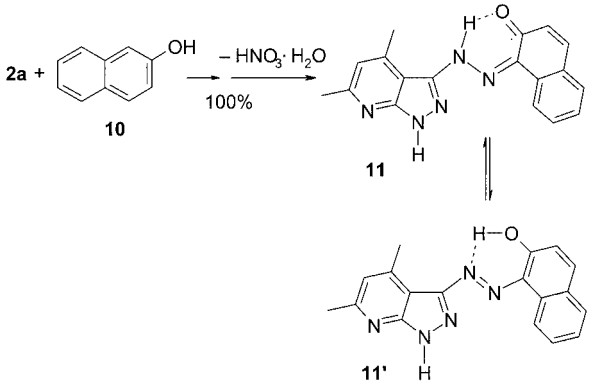
were confirmed by their IR, UV/Vis, NMR, MS, and HRMS spectra.

The **5**/**5′** tautomerism is clearly dominated by the barbituric acid moiety, and DFT calculations performed for related compounds in ref.[2] have the H-bridged hydrazono tautomer so much in favor over the azo form (> 13 kcal·mol^{-1}) that there cannot be any doubt that the molecular structure must be represented by **5** and not by **5′**.

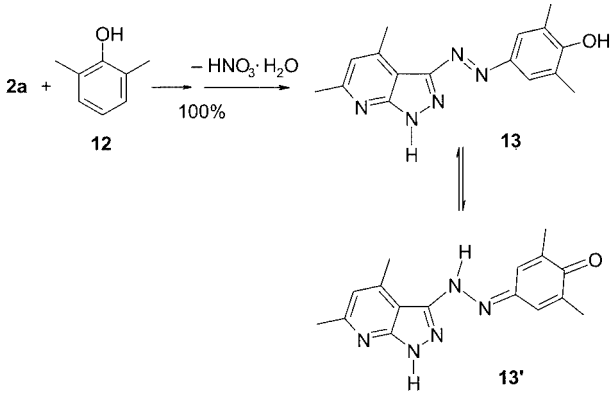
The azo coupling between **2a** and the open-chain C–H acidic *acetoacetanilide derivatives* **6a–e** did not stop at the salts **7**, but these cyclized directly to afford compounds **8** in an interesting solid-state cascade[18,19] to give the heterocyclic salts **8a–e** in waste-free fashion. The free pyridopyrazolo-triazines **9a–e** can be obtained from these in quantitative yield by the action of base. The pyrido[2′,3′:3,4]pyrazolo[5,1-*c*]triazine structure **9**[20] was established on the basis of the spectroscopic data. The IR spectra clearly indicate the lack of acetyl group absorptions in the $\tilde{\nu}$ = 1710–1715 cm^{-1} range and show the amide carbonyl group absorption (1698–1662 cm^{-1}). Furthermore, the MS and HRMS spectra corroborate the loss of water upon cyclization, and the other data (see Exp. Sect.) also support the structure **9**. The mild conditions for the cyclization with elimination in the crystal are indeed remarkable. These reactions are further examples of quantitative solid-state cascades with their extraordinary high atom economy and sustainability.[18,19]

Molecules with the heterocyclic system of **9** have been used as disperse dyes (for polyester, polyamide, acrylic fibers),[12] as antibacterial agents,[21] and as fungicides.[22] Our waste-free route to this system may therefore be of practical importance.

The *C*-couplings of solid diazonium salts **2** are not restricted to C-H acidic β-dicarbonyl compounds. The solid-state azo coupling between **2a** and β-naphthol or 2,6-dimethylphenol is preparatively useful and the "azo" dyes **11** or **13** are obtained in quantitative yield after neutralization (Scheme 4 and 5).



Scheme 4. Quantitative solid-state coupling between **2a** and β-naphthol **10**



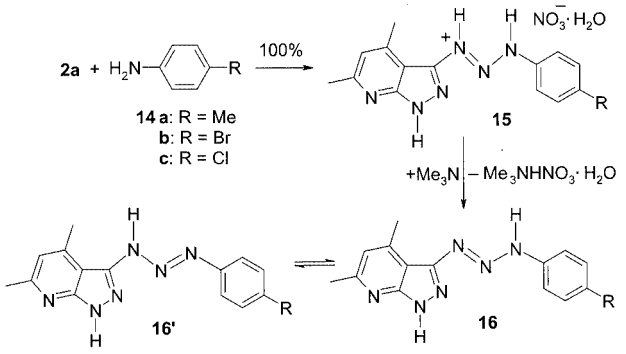
Scheme 5. Quantitative solid-state coupling between **2a** and 2,6-dimethylphenol **12**

The products **11** and **13** are characterized by their IR, MS, HRMS, and NMR spectra (see Exp. Sect.). According to DFT calculations at the B3LYP/6–31G* level, the hydrazono tautomer **11** is favored over **11′** by 2.1 kcal·mol^{-1}. As major entropy differences and crystal lattice effects are not to be expected here, this result should secure the formula **11**. In the case of **13**, however, the azo tautomer is found to be more stable than the hydrazono tautomer **13′**

by 3.6 kcal·mol^{-1}. It cannot be gauged whether this also holds for the crystalline state, because the lattice energy differences are not easily predictable. A previous analysis of closely related systems[23] did not consider ab initio DFT calculations.

Solid-State *N*-Coupling of 2a with Anilines

The success in the synthesis of various1,3-diaryltriazenes in ref.[2] prompted us also to make use of the advantages of solid-state reactions for the synthesis of 1-heteroaryl-3-aryltriazenes **16** from **2a**. Again, quantitative yields (of the salts **15**) were obtained by co-grinding of the anilines **14a**−**c** with **2a**, and the free triazenes **16** were quantitatively obtained from their salts by neutralization (Scheme 6).



Scheme 6. Quantitative solid-state syntheses of the tautomeric triazenes **16/16′**

The molecular structures **16** and **16′** are almost energetically equivalent according to DFT (B3LYP/6−31G*) calculations: the model **16** (R = H) is better by only 0.32, **16a′** is better by only 0.05, and **16c** is better by only 0.18 kcal·mol^{-1}. Unfortunately, the calculated azo bond frequencies (BLYP/6−31G**) also do not allow for distinction by IR spectroscopy. Clearly, almost 1:1 equilibria would be assumed in solution, and the tautomerism in the crystal would require a full X-ray crystal structure determination.

Interestingly, unlike 1,3-bisaryltriazenes,[1] the derivatives **16/16′** are stable in dilute methanol solution, so reliable UV/Vis spectra can be easily recorded. The λ_{max} values (368−370 nm) and high ε values point to the extended conjugation.

Discussion

Waste-free solid-state diazotizations and reactions of solid diazonium salts are very versatile and sustainable. They have now been extended to a highly complex heterocyclic system of practical importance. Numerous reactions of the diazonium salt **2a** have been successfully and quantitatively executed. Even cascade reactions were quantitative in the crystal. All of these reactions can be safely executed when precautionary measures are closely followed. Numerous derivatives with an interesting heterocyclic backbone are now easily and quantitatively obtained in stoichiometric runs. There can be no doubt that further extensions of this solid-state diazotization and coupling should be also useful for further heteroaromatic primary amines, because the techniques are very simple and permissive if the safety hints are fully acknowledged. Starting with pure reagents no purifying workup is required, and that feature is the most important advantage of the new technique for synthetic purposes. The formation of salts in this paper occurred with 100% yield in waste-free fashion. The neutralization of the salts with base does, of course, produce some inevitable waste in the form of salt solutions, but these do not constitute a major drawback, as the salts are only formed in stoichiometric quantities and with lowest environmental risk. The high atom economies and resource savings cannot be reached or topped by other techniques of syntheses, even if some minute solubility of the neutral products in water may require removal of very minor amounts of dissolved material from the salt solutions.

Experimental Section

Caution: Grinding of large amounts of solid diazonium salts may be hazardous to health. Solid diazonium salts explode upon being heated to their melting points and they are shock-sensitive (hammer and anvil test). Precautions should therefore be taken when handling these compounds. All reactions described here tend to be exothermic and must be properly slowed down as described in order to remove the heat of reaction efficiently. Solid diazonium salts must not be ground in mortars with sharp edges but only cautiously in agate mortars and pestles with smooth surfaces. In order to avoid any risk of explosion, we never used ball mills for grinding solid diazonium salts. No problems were experienced if the experimental conditions in this work were strictly followed. For violently reacting crystal mixtures, the single components should be ground separately, then carefully mixed, and left for reaction, during which ultrasound from room temperature cleaning baths may be applied.

The success of reaction was monitored by FT-IR spectroscopy in KBr. After disappearance of the diazonium band, the reaction time was extended by at least 10% to ensure completion of the process. The purity of the products was verified by thin layer chromatography, m.p. and ^{1}H NMR spectroscopy. The product yields were determined by weight. The experimental error was judged to be ±1%. The solid-state[1,2,9] and AFM[15−17] techniques have been described in detail elsewhere. Surface scraping was avoided,[15−17] and all supermicroscopic images were stable for at least 10 scans. Single crystals of **1a** were obtained from ethanol by slow evaporation. The size of the crystals used for Figure 1 and 2 was 3.3 × 0.4 × 0.05 mm^3. Diluted NO_2 gas in air was applied to the mounted single crystal by syringe from a distance of ca. 1 cm under a hood. After the specified exposure time, the gas was flushed away with a stream of air.

Vacuum tightness is essential in preparative gas-solid reactions, leakages must be sealed prior to the reaction. The NMR spectra (^{13}C in bb mode) were recorded with a Bruker WP 300, UV/ Vis spectra with a Perkin−Elmer Lambda 551 S, FT-IR spectra with a Perkin−Elmer 1720-X (not all frequencies are reported) and mass spectra with a Finnigan MAT212 instrument. B3LYP (basis set 6−31G*) and BLYP (basis set 6−31G**) DFT calculations with full geometry optimization were performed with the program TITAN, version 1.01, from Wavefunction, Inc., Irvine (USA).

Diazotization Procedure for 4,6-Dimethyl-1*H*-pyrazolo[3,4-*b*]pyridine-3-diazonium Nitrate Hydrate Derivatives 2: Compound **1** (2.00 mmol) was placed under vacuum in a 250 mL flask and then exposed to NO_2 (360 mg, 7.8 mmol) at 0.7 bar for 6 h at room temperature with occasional careful shaking. The excess gas was recovered from a trap at 77 K.

2a·H₂O: Yield 508 mg (100%); m.p. 143 °C (exploded). IR (KBr): $\tilde{\nu}$ = 3338, 3060, 2207 (N≡N⁺), 1636 (C=N), 1527, 1408, 1386, 1350, 1299, 1209, 1135, 1086, 1028, 954, 833 cm^{-1}. ^{1}H NMR (D_2O): δ = 2.75 (s, 6 H), 7.50 (s, 1 H) ppm. ^{13}C NMR (D2O): δ = 18.81, 20.39, 105.84, 118.58, 124.45, 124.87, 150.43, 156.60 ppm.

2b·H₂O: Yield 666 mg (100%); m.p. 133 °C (exploded). IR (KBr): $\tilde{\nu}$ = 3460, 2932, 2208 (N≡N⁺), 1627 (C=N), 1593, 1430, 1385, 1301, 1134, 1092, 1038, 1006, 837, 720 cm^{-1}. ^{1}H NMR (CF_3COOD): δ = 2.80 (s, 2 CH_3) ppm. ^{13}C NMR (CF_3COOD): δ = 21.14, 25.74, 112.93, 118.22, 125.71, 147.32, 149.77, 162.02 ppm.

Solid-State Preparation of 5-{(4,6-Dimethyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl)hydrazono}pyrimidine-2,4,6(1*H*,3*H*,5*H*)-triones 5a−c and -2-thioxo-pyrimidine-4,6(1*H*,3*H*,5*H*)-diones 5d−e: The (thio)-barbituric acid derivative **3** (1.00 mmol) was ground in an agate mortar. 4,6-Dimethyl-1*H*-pyrazolo[3,4-*b*]pyridine-3-diazonium nitrate hydrate **2** (1.00 mmol) was added and co-ground in five portions for 10 min each. The mixture was transferred to a 100 mL flask (by use of a horn-spoon and pencil), which was then evacuated. The mixture was exposed to $(CH_3)_3N$ (0.5 bar) for 12 h at room temperature. After condensation of the gas into a remote trap at 77 K, the trimethylammonium nitrate was washed away with water (20 mL) and the residual solid was dried.

5-{(4,6-Dimethyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl)hydrazono}-pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5a): Light yellow crystals; yield 301 mg (100%); m.p. > 300 °C. IR (KBr): $\tilde{\nu}$ = 1730, 1699, 1651, 1599, 1533, 1494, 1427, 1365, 1308, 1253, 1197, 1156, 885, 836, 807 cm^{-1}. UV (CH_3OH): λ_{max} (ε) = 381 (14200) nm. ^{1}H NMR ([D_6]DMSO): δ = 2.40 (s, 3 H), 2.60 (s, 3 H), 6.80 (s, 1 H), 11.20 (s, NH), 11.40 (s, NH), 13.30 (s, NH), 14.45 (s, NH) ppm. ^{13}C NMR ([D_6]DMSO): δ = 20.43, 24.13, 104.20, 118.56, 119.02, 142.05, 142.44, 149.74, 152.47, 159.33, 159.68, 162.52 ppm. MS: *m*/*z* (%) = 301 (100) [M⁺], 273 (18), 256 (20), 230 (14), 202 (24), 187 (18), 161 (20), 147 (34), 132 (37), 106 (18), 77 (20). HRMS calcd. for $C_{12}H_{11}N_7O_3$: 301.0923; found 301.0913.

1,3-Dimethyl-5-{(4,6-dimethyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl)-hydrazono}pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5b): Light yellow crystals; 330 mg (100%); m.p. > 300 °C. IR (KBr): $\tilde{\nu}$ = 1675, 1624, 1583, 1537, 1445, 1375, 1302, 1216, 1158, 1088, 1054, 864, 847, 741 cm^{-1}. UV (CH_3OH): λ_{max} (ε) = 376 (18800) nm. ^{1}H NMR (CF_3COOD): δ = 2.95 (s, 3 H), 3.05 (s, 3 H), 3.50 (s, 3 H), 3.55 (s, 3 H), 7.40 (s, 1 H) ppm. ^{13}C NMR (CF_3COOD): δ = 21.67, 22.05, 29.62, 30.91, 110.78, 122.69, 123.57, 144.48, 145.76, 153.89, 160.36, 161.26, 162.84, 163.66 ppm. MS: *m*/*z* (%) = 329 (100) [M⁺], 301 (18), 244 (4), 216 (4), 187 (38), 161 (30), 147 (38), 132 (38), 104 (10), 77 (10). HRMS calcd. for $C_{14}H_{15}N_7O_3$: 329.1236; found 329.1232.

5-{(4,6-Dimethyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl)hydrazono}-1,3-diphenyl-pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (5c): Light yellow crystals: 453 mg (100%); m.p. > 300 °C. IR (KBr): $\tilde{\nu}$ = 1730, 1693, 1635, 1536, 1490, 1445, 1385, 1300, 1223, 1102, 942, 834, 759, 694 cm^{-1}. UV (CH_3OH): λ_{max} (ε) = 371 (19000) nm. ^{1}H NMR (CF_3COOD): δ = 3.00 (s, 3 H), 3.10 (s, 3 H), 7.50 (br. s, 5 H), 7.65 (br. s, 6 H) ppm. ^{13}C NMR (CF_3COOD): δ = 19.91, 21.32, 110.42, 121.54, 121.77 (2 C), 128.68 (4 C), 130.88 (4 C), 131.52 (2 C), 132.50, 133.60, 143.13, 144.38, 152.84, 157.52, 159.78, 162.34 ppm. MS: *m*/*z* (%) = 453 (100) [M⁺], 425 (6), 306 (18), 257 (22), 214 (8), 187 (24), 147 (8), 132 (22), 119 (18), 77 (8). HRMS calcd. for $C_{24}H_{19}N_7O_3$: 453.1549; found 453.1547.

5-{(4,6-Dimethyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl)hydrazono}-2-thioxopyrimidine-4,6(1*H*,3*H*,5*H*)-dione (5d): Brown crystals; 311 mg (98%); m.p. > 300 °C. IR (KBr): $\tilde{\nu}$ = 1681, 1651, 1603, 1532, 1439, 1328, 1252, 1215, 1161, 1135, 1077, 876, 834, 799, 773 cm^{-1}. UV (CH_3OH): λ_{max} (ε) = 384 (22800) nm. ^{1}H NMR (CF_3COOD): δ = 2.95 (s, 3 H), 3.10 (s, 3 H), 7.40 (s, 1 H) ppm. ^{13}C NMR (CF_3COOD): δ = 19.99, 21.70, 110.01, 120.41, 121.42, 142.04, 144.12, 156.37, 158.56, 159.66, 160.23, 174.84 ppm. MS: *m*/*z* (%) = 317 (100) [M⁺], 219 (18), 187 (20), 179 (36), 162 (82), 147 (72), 132 (26), 119 (18), 77 (16). HRMS calcd. for $C_{12}H_{11}N_7O_2S$: 317.0694; found 329.0450.

1,3-Diethyl-5-{(4,6-dimethyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl)hydrazono}-2-thioxopyrimidine-4,6(1*H*,3*H*,5*H*)-dione (5e): Orange crystals; 370 mg (99%); m.p. > 300 °C. IR (KBr): $\tilde{\nu}$ = 1699, 1636, 1606, 1532, 1466, 1417, 1390, 1310, 1270, 1235, 1157, 1101, 909, 870, 810, 754 cm^{-1}. UV (CH_3OH): λ_{max} (ε) = 383 (26600) nm. ^{1}H NMR (CF_3COOD): δ = 1.35 (t, *J* = 7 Hz, 6 H), 2.95 (s, 3 H), 3.05 (s, 3 H), 4.60 (q, *J* = 7 Hz, 2 H), 4.61 (q, *J* = 7 Hz, 2 H), 7.35 (s, 1 H) ppm. ^{13}C NMR (CF_3COOD): δ = 11.68 (2 C), 20.21, 21.11, 43.77, 45.04, 109.22, 120.68, 122.20, 143.06, 143.28, 157.03, 158.26, 158.98, 159.64, 176.12 ppm. MS: *m*/*z* (%) = 373 (100) [M⁺], 340 (18), 242 (8), 212 (8), 187 (48), 162 (8), 132 (18), 106 (6), 86 (14). HRMS calcd. for $C_{16}H_{19}N_7O_2S$: 373.1320; found 373.1321.

Solid-State Preparation of Pyrido[2′,3′:3,4]-1*H*-pyrazolo[5,1-*c*]-[1,2,4]triazine Derivatives (9): The acetoacetanilide derivative **6** (2.00 mmol) was ground in an agate mortar. 4,6-Dimethyl-1*H*-pyrazolo[3,4-*b*]pyridine-3-diazonium nitrate hydrate **2a** (2.00 mmol) was added and co-ground in five portions for 10 min each. The mixture was transferred to a 100 mL flask, which was then evacuated. The mixture was exposed to $(CH_3)_3N$ (0.5 bar) for 12 h at room temperature. After condensation of the gas into a remote trap at 77 K, the trimethylammonium nitrate was washed away with water (20 mL) and the residual solid dried.

Compound 9a: Yield 664 mg (100%); m.p. 273 °C. IR (KBr): $\tilde{\nu}$ = 3344, 1690, 1613, 1595, 1535, 1445, 1314, 1190, 1109 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ = 2.80 (s, 3 H), 3.10 (s, 3 H), 3.55 (s, 3 H), 7.15 (pseudo-t, 1 H), 7.20 (s, 1 H), 7.35 (pseudo-t, 2 H), 7.75 (pseudo-d, 2 H), 10.30 (br. s, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.89, 19.31, 25.78, 105.20, 119.86 (2 C), 121.36, 124.79, 129.10 (2 C), 136.68, 137.32, 138.57, 144.82, 145.00, 160.58, 161.53, 166.17 ppm. MS: *m*/*z* (%) = 332 (100) [M⁺], 315 (44), 262 (4), 240 (44), 198 (6), 186 (48), 166 (6), 144 (6), 131 (28), 93 (14), 77 (16). HRMS calcd. for $C_{18}H_{16}N_6O$: 332.1385; found 332.1386.

Compound 9b: Yield 684 mg (99%); m.p. 286 °C. IR (KBr): $\tilde{\nu}$ = 3343, 3087, 1682, 1657, 1592, 1531, 1406, 1313, 1198, 1140, 951, 816 cm^{-1}. ^{1}H NMR ($CDCl_3$/CF_3COOH): δ = 2.40 (s, 3 H), 3.05 (s, 3 H), 3.40 (s, 3 H), 3.55 (s, 3 H), 7.25 (pseudo-d, 2 H), 7.50 (pseudo-d, 2 H), 7.60 (s, 1 H), 10.30 (s, NH) ppm. ^{13}C NMR ($CDCl_3$/CF_3COOD): δ = 14.06, 20.64, 20.86, 21.05, 109.12, 121.22, 122.19 (2 C), 130.14 (2 C), 132.61, 137.49, 140.63, 142.06, 145.24, 151.09, 160.30, 160.47, 201.55 ppm. MS: *m*/*z* (%) = 346 (100) [M⁺], 329 (20), 276 (4), 240 (10), 186 (24), 173 (4), 144 (6), 131 (8), 107 (12), 67(8). HRMS calcd. for $C_{19}H_{18}N_6O$: 346.1542; found 346.1533.

Compound 9c: Yield 715 mg (99%); m.p. 254 °C. IR (KBr): $\tilde{\nu}$ = 3335, 3150, 2969, 1677, 1662, 1595, 1533, 1514, 1413, 1369, 1312,

1251, 1183, 1107, 846 cm^{-1}. ^1H NMR ($CDCl_3/CF_3COOH$): δ = 3.00 (s, 3 H), 3.30 (s, 3 H), 3.55 (s, 3 H), 3.80 (s, 3 H), 6.90 (pseudo-d, 2 H), 7.50 (s, 1 H), 7.55 (pseudo-d, 2 H), 10.10 (br. s, NH) ppm. MS: *m/z* (%) = 362 (100) [M^+], 330 (6), 240 (12), 186 (25), 123 (13). HRMS calcd. for $C_{19}H_{18}N_6O_2$: 362.1491; found 362.1492.

Compound 9d: Yield 754 mg (100%); m.p. > 300 °C. IR (KBr): ṽ = 3341, 3065, 1698, 1608, 1592, 1510, 1408, 1370, 1341, 1313, 1183, 1111, 1052, 857, 752, 669 cm^{-1}. ^1H NMR ($CDCl_3/CF_3COOH$): δ = 3.05 (s, 3 H), 3.35 (s, 3 H), 3.55 (s, 3 H), 7.50 (s, 1 H), 7.90 (pseudo-d, 2 H), 8.20 (pseudo-d, 2 H), 10.55 (br. s, NH) ppm. MS: *m/z* (%) = 377 (100) [M^+], 314 (12), 240 (36), 186 (21), 131 (38), 67 (22). HRMS calcd. for $C_{18}H_{15}N_7O_3$: 377.1236; found 377.1237.

Compound 9e: Yield 822 mg (100%); m.p. > 300 °C. IR: ṽ = 3138, 3092, 1662, 1593, 1521, 1487, 1396, 1358, 1294, 1258, 1199, 1148, 1081, 956, 916, 820, 777 cm^{-1}. ^1H NMR ($CDCl_3/CF_3COOH$): δ = 3.05 (s, 3 H), 3.35 (s, 3 H), 3.55 (s, 3 H), 7.40−7.60 (m, 5 H), 10.35 (br. s, NH) ppm. MS: *m/z* (%) = 412 (100) [M^+], 410 (98) [M^+], 314 (60), 240 (60), 186 (58), 131 (54). HRMS calcd. for $C_{18}H_{15}{}^{79}BrN_6O$: 410.0490; found 410.0486. HRMS calcd. for $C_{18}H_{15}{}^{81}BrN_6O$: 412.0470; found 412.0469.

Compound 9f: Yield 732 mg (100%); m.p. 300 °C. IR (KBr): ṽ = 3135, 3095, 1662, 1592, 1526, 1489, 1402, 1359, 1312, 1256, 1195, 1148, 1082, 1012, 951, 918 cm^{-1}. ^1H NMR ($CDCl_3/CF_3COOH$): δ = 3.05 (s, 3 H), 3.30 (s, 3 H), 3.55 (s, 3 H), 7.30 (pseudo-d, 2 H), 7.50 (s, 1 H), 7.60 (pseudo-d, 2 H), 10.20 (br. s, NH) ppm. MS: *m/z* (%) = 367 (25) [M^+], 366 (100) [M^+], 349 (12), 314 (37), 240 (50), 198 (4), 186 (48), 157 (4), 144 (12), 131 (41), 104 (17), 77 (10), 67 (22). HRMS calcd. for $C_{18}H_{15}ClN_6O$: 366.0995; found 366.0996.

Coupling between 2a and the Phenols 10 and 12: β-Naphthol (**10**, 432 mg, 3.00 mmol) or 2,6-dimethylphenol (**12**, 336 mg, 3.00 mmol) was ground in an agate mortar. 4,6-Dimethyl-1*H*-pyrazolo[3,4-*b*]pyridine-3-diazonium nitrate hydrate **2a** (762 mg, 3.00 mmol) was added in five portions and co-ground for 10 min. After transfer of the incompletely reacted mixture to a test tube and application of ultrasound (from a cleaning bath) overnight the diazonium band in the IR had disappeared. The solid material was washed with 0.5 N NaOH (20 mL) and cold water and dried.

Naphthalene-1,2-dione 1-[(4,6-dimethyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl)hydrazone] (11):[23] Dark red crystals: (950 mg, 100%); m.p. 312 °C (after dec. from ca. 200 °C). IR (KBr): ṽ = 1613, 1595, 1511, 1450, 1412, 1379, 1304, 1250, 1208, 1184, 1148, 1107, 826, 765, 616 cm^{-1}. ^1H NMR (orange solution in CF_3COOD): δ = 2.80 (s, 3 H), 2.95 (s, 3 H), 6.60 (m, 1Ar-H), 7.15 (m, 1Ar-H), 7.40 (m, 3Ar-H), 7.75 (m, 1Ar-H), 8.35 (m, 1Ar-H). MS: *m/z* (%) = 317 (88) [M^+], 288 (100), 260 (63), 233 (4), 156 (6), 147 (8), 143 (32), 128 (34), 115 (63), 77 (18). HRMS calcd. for $C_{18}H_{15}N_5O$: 317.1276; found 317.1278.

4-{(4,6-Dimethyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl)diazenyl}-2,6-dimethylphenol (13): Glossy, light brown crystals, yield 870 mg (98%); m.p. 278 °C (dec.). IR (KBr): ṽ = 1614, 1592, 1480, 1440, 1382, 1297, 1266, 1237, 1208, 1122, 1027, 888, 810 cm^{-1}. ^1H NMR (blood-red solution in CF_3COOD): δ = 2.51 (s, 6 H), 3.08 (s, 3 H), 3.17 (s, 3 H), 7.69 (s, 1 H), 8.18 (s, 2 H) ppm. ^{13}C NMR (CF_3COOD): δ = 15.03 (2 C), 19.91, 20.13, 115.46, 123.33, 128.28 (2 C), 130.62 (2 C), 138.32, 144.16, 149.86, 157.74, 160.44, 166.99 ppm. MS: *m/z* (%) = 295 (100) [M^+], 267 (44), 240 (16), 146 (5), 121 (96), 91 (22), 77 (24). HRMS calcd. for $C_{16}H_{17}N_5O$: 295.1433; found 295.1434.

Synthesis of (4,6-Dimethyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl)aryltriazenes (16): Substituted solid anilines (1.00 mmol) were ground in an agate mortar. The diazonium nitrate hydrate **2a** (1.00 mmol) was then added in five portions and co-ground for 10 min. The mixture was transferred to a 100 mL flask, which was then evacuated. The mixture was exposed to $(CH_3)_3N$ (0.5 bar) for 12 h at room temperature. After condensation of the gas into a remote trap at 77 K, the trimethylammonium nitrate was washed away with water (20 mL) and the residual solid was dried.

4,6-Dimethyl-3-[3-(4-methylphenyl)triaz-1-enyl]-1*H*-pyrazolo[3,4-*b*]-pyridine (16a): Orange crystals, yield 280 mg (100%); m.p. 173 °C. IR (KBr): ṽ = 3150, 3093, 2986, 2921, 1613, 1532, 1425, 1296, 1253, 1194, 1148, 833 cm^{-1}. UV (CH_3OH): λ_{max} (ε) = 370 (19300) nm. ^1H NMR ($CDCl_3$): δ = 2.20 (s, 3 H), 2.40 (s, 3 H), 2.50 (s, 3 H), 6.75 (s, 1 H), 7.05 (pseudo-d, 2 H), 7.15 (pseudo-d, 2 H), 12.35 (s, 1 NH), 13.05 (s, 1 NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 19.72, 20.33, 24.08, 106.55, 114.32, 118.35, 129.75 (3 C), 131.51, 139.02, 142.19, 150.98, 152.61, 158.11 ppm. MS: *m/z* (%) = 280 (M^+,4), 252 (86), 236 (4), 223 (4), 174 (8), 162 (36), 146 (20), 119 (76), 107 (60), 91 (100), 65 (28). HRMS calcd. for $C_{15}H_{16}N_6$: 280.1436; found 280.1436.

3-(4-Bromophenyl)-1-(4,6-dimethyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl)-triazene (16b): Yellow crystals: 345 mg (100%); m.p. 191 °C. IR (KBr): ṽ = 3140, 3080, 2977, 2932, 1598, 1524, 1488, 1428, 1288, 1250, 1195, 1174, 1153, 1070, 830 cm^{-1}. UV (CH_3OH): λ_{max} (ε) = 368 (20400) nm. ^1H NMR ($CDCl_3/CF_3COOD$): δ = 2.85 (s, 3 H), 2.90 (s, 3 H), 7.25 (s, 1 H), 8.05 (d, 2 H), 8.30 (d, 2 H) ppm. ^{13}C NMR ($CDCl_3/CF_3COOD$): δ = 19.29, 19.87, 107.07, 111.20, 119.35, 132.61 (2 C), 135.90 (2 C), 141.18, 142.91, 147.75, 158.71, 161.67 ppm. MS: *m/z* (%) = 346 (4) [M^+], 344 (4) [M^+], 318 (62), 316 (64), 238 (5), 236 (5), 185 (55), 183 (55), 157 (98), 155 (100), 146 (38), 119 (26), 106 (16), 78 (32). HRMS calcd. for $C_{14}H_{13}{}^{79}BrN_6$: 344.0385; found 344.0386. HRMS calcd. for $C_{14}H_{13}{}^{81}BrN_6$: 346.0365; found 346.0368.

1-(4,6-Dimethyl-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl)-3-(4-chlorophenyl)-triazene (16c): Yellow crystals, yield 300 mg (100%); m.p. 184 °C. IR: ṽ = 3142, 3088, 2984, 2934, 1601, 1526, 1493, 1430, 1285, 1250, 1194, 1172, 1154, 1090, 831 cm^{-1}. UV (CH_3OH): λ_{max} (ε) = 369 (26300) nm. ^1H NMR ($CDCl_3/CF_3COOD$): δ = 2.80 (s, 3 H), 2.95 (s, 3 H), 7.25 (s, 1 H), 7.85 (d, 2 H), 8.40 (d, 2 H) ppm. ^{13}C NMR ($CDCl_3/CF_3COOD$): δ = 19.33, 19.85, 107.02, 110.52, 119.71, 132.81 (2 C), 133.11 (2 C), 142.41, 147.66, 151.95, 158.99, 161.41 ppm. MS: *m/z* (%) = 300 (M^+,6), 272 (98), 237 (4), 174 (52), 162 (74), 139 (92), 111 (100), 78 (26). HRMS calcd. for $C_{14}H_{13}ClN_6$: 300.0890; found 300.0893.

[1] G. Kaupp, A. Herrmann, *J. Prakt. Chem.* **1997**, *339*, 256−260.
[2] G. Kaupp, A. Herrmann, J. Schmeyers, *Chem. Eur. J.* **2002**, *8*, 1359−1406.
[3] [3a] M. P. Wentland, R. B. Permi, J. Huang, R. G. Powles, S. C. Aldous, K. M. Klingbeil, A. D. Peverly, R. G. Robinson, T. H. Corbett, *Bioorg. Med. Chem. Lett.* **1996**, *6*, 1345−1350. [3b] C. D. Benham, T. P. Blackburn, A. Johns, N. R. Kotecha, R. T. Martin, D. R. Thomas, M. Thompson, R. W. Ward, *Bioorg. Med. Chem. Lett.* **1995**, *5*, 2455−2460.
[4] H. A. Soleiman, A. K. Khalafallah, H. M. Abdelzaher, *J. Chinese Chem. Soc. (Taipei)* **2000**, *47*, 1267−1272.
[5] I. T. Forbes, C. N. Johnson, G. E. Jones, J. Loudon, J. M. Nicholass, M. Thompson, N. Upton, *J. Med. Chem.* **1990**, *33*, 2640−2645.
[6] G. A. Geselbracht, Belg. Pat. **1964**, 652,691 (to Martin-Marietta Corp.); *Chem. Abstr.* **1966**, *64*, 52521.
[7] W. Steinemann, Swiss. Pat. **1965**, 386,591 (to Sandoz A. G.); *Chem. Abstr.* **1965**, *63*, 32241.

[8] E. Fleckenstein, R. Mohr, *Ger. Offen*, **1974**, 2,305,617 (to Hoechst AG); *Chem. Abstr.* **1975**, *82*, 45009.
[9] G. Kaupp, J. Schmeyers, M. Haak, T. Marquardt, A. Herrmann, *Mol. Cryst. Liq. Cryst.* **1996**, *276*, 315−337.
[10] A. M. K. El-Dean, A. A. Geies, T. A. Mohamed, *Indian J. Chem. Sect. B* **1991**, *30*, 878−882.
[11] M. Lacan, K. Tabakovic, *Croat. Chim. Acta* **1975**, *47*, 127−133.
[12] E. Fleckenstein, R. Mohr (to Hoechst A. G.) DE 2238400, **1974**; *Chem. Abstr.* **1975**, *81* 65179; DE 2355967, **1974**; *Chem. Abstr.* **1975**, *83*, 207573.
[13] A. M. K. El-Dean, T. A. Mohamed, A. A. Geies, *Z. Naturforsch., Teil B* **1991**, *46*, 541−546.
[14] B. M. Lynch, M. A. Khan, H. C. Teo, F. Pedrotti, *Can. J. Chem.* **1988**, *66*, 420−428.
[15] [15a] G. Kaupp, *Supermicroscopy in Supramolecular Chemistry: AFM, SNOM, and SXM*, in *Comprehensive Supramolcular Chemistry*, vol. 8 (Eds.: J. L. Atwood, J. E. D. Davies, D. D. MacNicol, F. Vögtle, J.-M. Lehn, J. A. Ripmeester), Elsevier, Oxford, **1996**, p. 381−423. [15b] G. Kaupp, *Chem. Unserer Zeit* **1997**, *31*, 129−139.
[16] G. Kaupp, J. Schmeyers, U. Pogodda, M. Haak, T. Marquardt, M. Plagmann, *Thin Solid Films* **1995**, *264*, 205−211.
[17] [17a] G. Kaupp, *J. Vac. Sci. Technol. B* **1994**, *12*, 1952−1956; G. Kaupp, M. Plagmann, *J. Photochem. Photobiol. A* **1994**, *80*, 399−407. [17b] G. Kaupp, *Mol. Cryst. Liq. Cryst.* **1994**, *242*, 153−169.
[18] [18a] G. Kaupp, M. R. Naimi-Jamal, *Eur. J. Org. Chem.* **2002**, 1368−1373. [18b] G. Kaupp, M. R. Naimi-Jamal, J. Schmeyers, *Chem. Eur. J.* **2002**, *8*, 594−600.
[19] G. Kaupp, J. Schmeyers, A. Kuse, A. Atfeh, *Angew. Chem. Int. Ed.* **1999**, *38*, 2896−2899.
[20] Similar compounds were described: M. Kocevar, B. Stanovnik, M. Tisler, *J. Heterocycl. Chem.* **1978**, *15*, 1175−1184.
[21] M. Z. A. Badr, A. A. Geies, M. S. Abbady, A. A. Dahy, *Afinidad* **2001**, *58*, 380−384.
[22] M. A. A. Elneairy, F. A. Attaby, M. S. Elsayed, *Phosphorus, Sulfur Silicon Relat. Elem.* **2000**, *167*, 161−179.
[23] S. A. Ibrahim, A. M. Hammam, A. M. K. El-Dean, A. A. Mohamed, N. M. Rageh, *Can. J. Appl. Spectrosc.* **1993**, *38*, 1−6.

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