Notiz / Note

Synthesis of Novel Heteroaromatic Polyfused *as*-Triazines by Ring Transformation[1]

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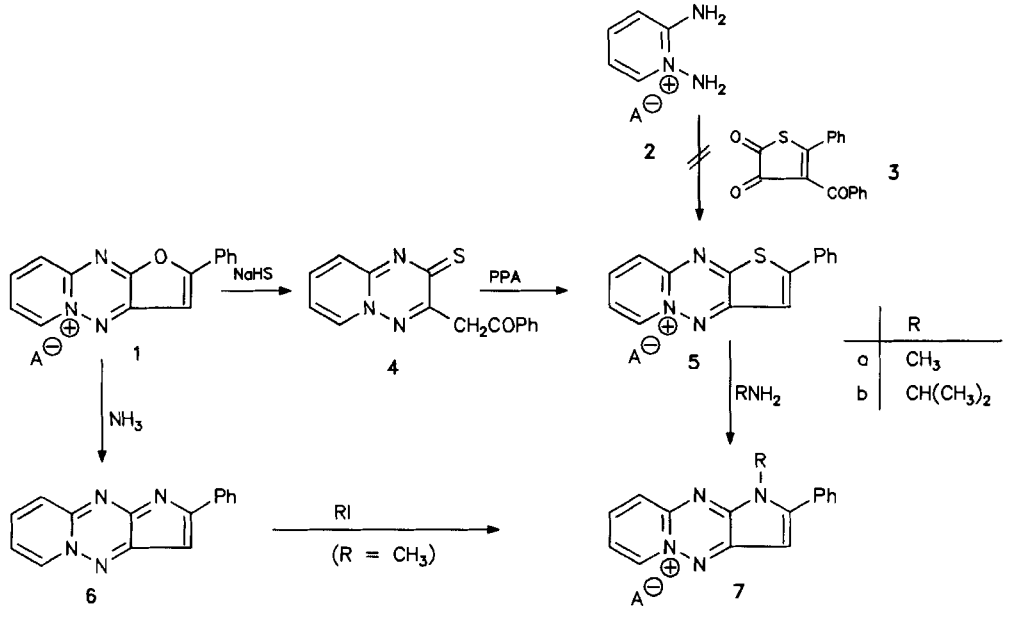
Ring transformation of the tricyclic furo-fused *as*-triazinium salt **1** in the presence of nucleophilic reagents (e.g. sodium hydrogensulfide, sodium salts of malonic ester, ethyl cyanoacetate, acetylacetone, dimedone, or malononitrile) leads to the two new heteroaromatic ring systems thieno[2,3-*e*]pyrido[1,2-*b*]-*as*-triazinium salt (**5**) and differently substituted cyclopenta[*e*]pyrido[1,2-*b*]-*as*-triazine compounds (**8**, **9**, **10**, **11**, and **13**).

Recently, we have reported[2,3] that the tricyclic furo[2,3-*e*]pyrido[1,2-*b*]-*as*-triazinium salt **1** readily reacts with nitrogen nucleophiles to give colored ring transformation products (e.g., reaction of **1** with ammonia leads to the red pyrrolo[2,3-*e*]pyrido[1,2-*b*]-*as*-triazine **6**).

As a continuation of these studies we have found now that this type of ring transformations can be extended also to reactions with sulfur and carbon nucleophiles which can result in derivatives of novel polyfused heteroaromatic ring systems. We were particularly interested in this methodology as our earlier efforts to realize a direct synthesis of the thieno compound **5** – analogously to the preparation of related compounds[2,4] (i.e. by condensation of diaminopyridinium salt **2** with the corresponding thiophenedione reagent **3**) – failed.

We have found that the tricyclic furo-fused salt **1** easily reacts with sodium hydrogen sulfide at room temperature to afford the ring-opened thione **4** which undergoes ring closure by treatment with polyphosphoric acid to give the thieno-fused salt **5** in good yield. The new heteroaromatic salt 2-phenylthieno[2,3-*e*]pyrido[1,2-

Scheme 1



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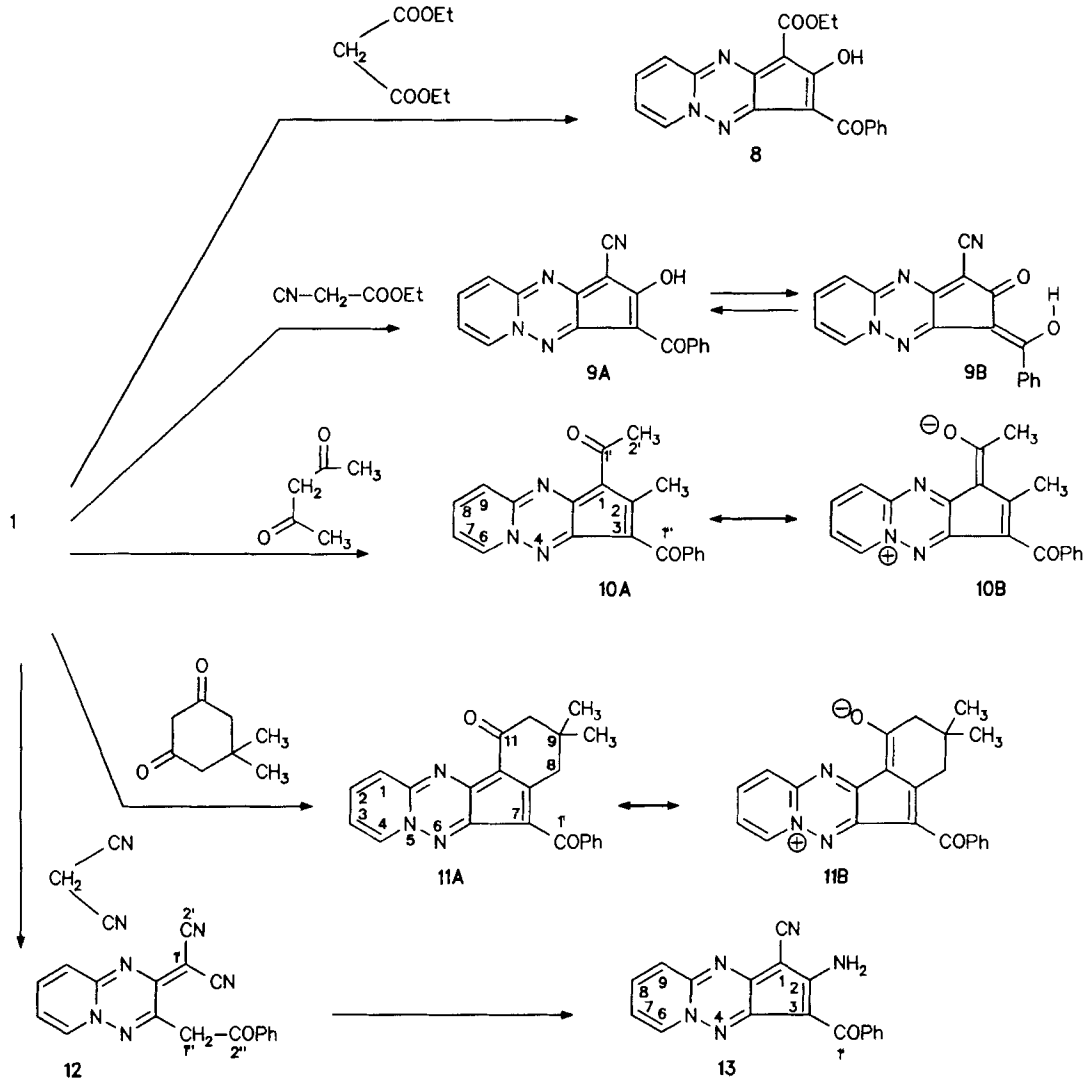
Scheme 2



b]-*as*-triazinium perchlorate (**5**) seems also to be reactive towards nucleophiles.

Thus, reaction of **5** with a primary amine (e.g. with isopropylamine or methylamine) affords the 1-substituted pyrrolo-fused salt **7**. This approach to the quaternary salt **7** nicely completes the earlier elaborated[5] synthetic pathway of quaternization of the neutral pyrrolo-fused tricycle **6**.

Furthermore, the successful ring transformation with hydrogen sulfide has prompted us to extend our studies to carbon nucleophiles, too[6]. According to our expectations, the anion generated from malonic ester reacts easily with **1** with formation of the derivative **8** of a hitherto unknown heteroaromatic ring system, i.e. cyclopenta[*e*]pyrido[1,2-*b*]-*as*-triazine. Also, cyanoacetic acid ester, acetylacetone, and dimedone (5,5-dimethylcyclohexane-1,3-dione) react analogously to yield derivatives **9**, **10**, and **11**, respectively. Furthermore, ring transformation has been observed on treatment with malononitrile with the difference that, in this case, the ring-opened intermediate **12** is first isolated which, under reflux conditions, undergoes ring closure to derivative **13**. Ring-opened compounds of type **12** should also be non-isolable intermediates during reactions of **1** leading to the cyclocondensation products **9**, **10**, **11**.

The structures of all the new ring transformation products have been satisfactorily supported by routine analytical (NMR, IR, MS) methods. It is interesting to note that compound **9** seems to exist rather in the **9B** than **9A** tautomeric form as indicated by its carbonyl ^{13}C-NMR shift value (δ = 177.56, in contrast to a value above δ = 190 which has been found for the benzoyl carbonyl of **11**). Furthermore, a comparison of the color of the five new cyclopenta-fused derivatives shows that compounds **10** and **11** are red, whereas derivatives **8**, **9**, and **13** are yellow. The significant bathochromic shift in the case of **10** and **11** is probably due to the enhanced delocalization of the π-electronic system which is illustrate by the valence bond structures **A** and **B** in both cases.

A quantitative interpretation of the appearance of the deep color of these derivatives and related compounds is in progress and will soon be published.

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Experimental

Melting points (uncorrected): Büchi apparatus. – IR: Nicolet 205 FT IR. – NMR: Varian XL-400; TMS as internal standard. – MS: AEI MS-902.

2-(Benzoylmethyl)-2H-pyrido[1,2-b]-as-triazine-2-thione (**4**): A suspension of 2-phenylfuro[2,3-*e*]pyrido[1,2-*b*]-*as*-triazinium perchlorate (**1**, 0.35 g, 1.0 mmol) in methanol (10 ml) was treated with a methanolic solution of sodium hydrogen sulfide (0.2 g). Within a few min, a deeply colored solid precipitated which was filtered off and dried to give 0.22 g (77%) of thione **4**; m.p. 225–227°C. – IR (KBr): $\tilde{\nu}$ = 3100 cm^{-1}, 3060, 3030, 3000, 2950, 1680, 1630, 1570, 1530, 1470, 1440, 1380, 1290, 1270, 1200, 1140, 790, 690. – $C_{15}H_{11}N_3OS$ (281.3): calcd. C 64.05, H 3.94, N 14.94, S 11.38; found C 63.92, H 3.82, N 14.97, S 11.42.

2-Phenylthieno[2,3-e]pyrido[1,2-b]-as-triazinium Perchlorate (**5**, A = ClO_4): A mixture of **4** (0.56 g, 2.0 mmol) and polyphosphoric acid (10 g) was stirred at 140–150°C for 2 h. The crude slurry was diluted with ice/water (40 ml) and then treated with 70% perchloric acid (1 ml) yielding a yellow precipitate. Filtration, washing with ethyl acetate, and recrystallization from nitromethane/ethyl acetate gave 0.51 g (70%) of perchlorate **5**; m.p. >300°C. – IR (KBr): $\tilde{\nu}$ = 3090 cm^{-1}, 3060, 3020, 3000, 1620, 1570, 1530, 1490, 1470, 1440, 1420, 1380, 1270, 1250, 1220, 1180, 1150, 1100, 1080, 840, 790, 770, 680, 620. – ^{1}H NMR (CD_3CN): δ = 9.36 (m, 1H, 6-H, J_o = 7, J_m = 1.5 Hz), 8.71 (m, 1H, 8-H, J_o = 8.5 and 7, J_m = 1.5 Hz), 8.57 (m, 1H, 9-H, J_o = 8.5, J_m = 1.5 Hz), 8.26 (m, 1H, 7-H, J_o = 7 and 7, J_m = 1.5 Hz), 8.12 (s, 1H, 3-H), 8.06 and 7.70 (m, 5H, 2′-, 3′-, 4′-, 5′-, 6′-H). – $C_{15}H_{10}ClN_3O_4S$ (363.8): calcd. C 49.52, H 2.77, N 11.55; found C 49.12, H 2.82, N 11.52.

1-Isopropyl-2-phenyl-1H-pyrrolo[2,3-e]pyrido[1,2-b]-as-triazinium Perchlorate (**7b**, A = ClO_4): Perchlorate **5** (0.36 g, 1.0 mmol) was suspended in acetonitrile (5 ml), and the suspension was treated with isopropylamine (0.15 ml). A deep red solution was formed immediately from which yellow crystals separated. Filtration of this solid and recrystallization from acetonitrile/ether gave 0.23 g (58%) of **7b**; m.p. 246–248°C. – IR (KBr): $\tilde{\nu}$ = 3130 cm^{-1}, 3100, 3070, 3040, 2990, 1610, 1550, 1480, 1440, 1370, 1270, 1250, 1090, 790, 770, 700, 620. – ^{1}H NMR (CD_3CN): δ = 9.20 (m, 1H, 6-H, J_o = 7, J_m = 1.8 Hz), 8.48 (m, 1H, 8-H, J_o = 8.5 and 7, J_m = 1.8 Hz), 8.40 (m, 1H, 9-H, J_o = 8.5, J_m = 1.8 Hz), 8.00 (m, 1H, 7-H, J_o = 7 and 7, J_m = 1.8 Hz), 7.71 (m, 5H, 2′-, 3′-, 4′-, 5′-, 6′-H), 7.08 (s, 1H, 3-H), 4.82 [m, 1H, C*H*(CH_3)$_2$], 1.78, 176 [d, 6H, CH(CH_3)$_2$, J = 8 Hz]. – $C_{18}H_{17}ClN_4O_4$ (388.5): calcd. C 55.60, H 4.37, N 14.41; found C 55.53, H 4.32, N 14.48.

1-Methyl-2-phenyl-1H-pyrrolo[2,3-e]pyrido[1,2-b]-as-triazinium Tetrafluoroborate (**7a**, A = BF_4) was obtained from the perchlorate **5** (A = ClO_4) by using methylamine according to the previous procedure. The product, 0.18 g (50%), proved to be totally identical with that prepared from **6** and methyl iodide[5].

General Procedure for Preparation of Ring Transformation Products **8–11** *and Ring-opened Compound* **12**: The sodium salts of the reagents were generated as follows: To a solution of the appropriate reagent (3 mmol) in acetonitrile (5 ml) sodium hydride (commercially available as a 50% suspension, 0.1 g, 2 mmol) was added and the mixture was stirred at room temp. for 10 min. To the mixture was added 2-phenylfuro[2,3-*e*]pyrido[1,2-*b*]-*as*-triazinium perchlorate (**1**, 0.35 g, 1.0 mmol), and the reaction mixture was stirred at room temp. for 5 h. The precipitated products were filtered off, washed with petroleum ether and recrystallized from the given solvent.

Ethyl 3-Benzoyl-2-hydroxycyclopenta[e]pyrido[1,2-b]-as-triazine-1-carboxylate (**8**): M.p. 220–225°C (ethanol/acetic acid). Yield: 0.20 g (55%). – IR (KBr): $\tilde{\nu}$ = 3110 cm^{-1}, 3095, 3060, 2950, 2920, 2850, 1680, 1640, 1600, 1530, 1510, 1470, 1420, 1410, 1380, 1360, 1260, 1210, 1130, 1080, 1060, 1030, 790, 780, 770, 700. – UV (acetonitrile): λ_{max} (lg ε) = 270 nm (4.484), 318 (4.446). – ^{1}H NMR ($CDCl_3$): δ = 8.35 (d, 1H, 6-H, J_o = 7, J_m = 1.5 Hz), 8.0 (m, 1H, 9-H, J_o = 8, J_m = 1.8 Hz), 7.99 (m, 2H, 3′-, 7′-H), 7.87 (m, 1H, 8-H, J_o = 8 and 7, J_m = 1.5 Hz), 7.59 (m, 1H, 5′-H), 7.51 (m, 2H, 4′-, 6′-H), 7.27 (m, 1H, 7-H, J_o = 7 and 7, J_m = 1.8 Hz), 4.48 (m, 2H, CH_2CH_3), 1.48 (t, 3H, CH_2CH_3). – $C_{20}H_{15}N_3O_4$ (361.4): calcd. C 66.47, H 4.18, N 11.63; found C 66.43, H 4.25, N 11.60. – Mol. mass 361 (MS).

3-Benzoyl-2-hydroxycyclopenta[e]pyrido[1,2-b]-as-triazine-1-carbonitrile (**9**): M.p. >250°C (acetonitrile/acetic acid). Yield: 0.17 g (54%). – IR (KBr): $\tilde{\nu}$ = 3460 cm^{-1}, 3110, 3070, 3060, 3030, 2210, 1580, 1530, 1480, 1450, 1390, 1300, 1255, 1210, 1170, 1150, 1120, 1055, 1000, 970, 770, 755, 690, 680. – UV (acetonitrile): λ_{max} (lg ε) = 256 nm (4.593), 322 (4.530). – ^{1}H NMR ($CDCl_3$/[D_6]DMSO): δ = 8.56 (d, 1H, 6-H), 8.09 (m, 1H, 8-H), 8.08 (m, 2H, 3′-, 7′-H), 7.93 (m, 1H, 9-H), 7.66 (m, 1H, 5′-H), 7.58 (m, 2H, 4′-, 6′-H), 7.48 (m, 1H, 7-H). – ^{13}C NMR ($CDCl_3$/[D_6]DMSO): δ = 184.05 (C-2), 177.56 (C-1′), 148.5, 145.51, 139.76 (C-3a, -9a, -10a), 132.0, 131.93, 126.57 (C-6, -5′, -8), 131.75 (C-2′), 123.49 (C-3′), 121.90 (C-4′), 119.49, 111.75 (C-9, -7), 107.54 (C-3), 107.51 (CN), 91.07 (C-1). – $C_{18}H_{10}N_4O_2$ (314.3): calcd. C 68.78, H 3.20, N 17.83; found C 68.76, H 3.25, N 17.53. – Mol. mass 314 (MS).

1-Acetyl-3-benzoyl-2-methylcyclopenta[e]pyrido[1,2-b]-as-triazine (**10**): M.p. >250°C (acetonitrile/acetic acid). Yield: 0.20 g (61%). – IR (KBr): $\tilde{\nu}$ = 3110 cm^{-1}, 3080, 3030, 1640, 1610, 1600, 1570, 1550, 1470, 1430, 1400, 1350, 1270, 1250, 1200, 1160, 1140, 1100, 1020, 840, 760, 735, 720, 700, 640. – UV (chloroform): λ_{max} (lg ε) = 258 nm (4.425), 292 (4.557), 398 (3.978), 518 (3.217). – ^{1}H NMR ($CDCl_3$/TFA): δ = 8.64 (m, 1H, 6-H, J_o = 7, J_m = 1.5 Hz), 8.10 (m, 1H, 9-H, J_o = 8.5, J_m = 1.8 Hz), 7.99 (m, 1H, 8-H, J_o = 8.5 and 6.8, J_m = 1.5 Hz), 7.74, 7.45 (m, 5H, 3″-, 4″-, 5″-, 6″-, 7″-H), 7.45 (m, 1H, 7-H, J_o = 7 and 6.8, J_m = 1.8 Hz), 3.04 (s, 3H, $COCH_3$), 2.87 (s, 3H, CH_3). – ^{13}C NMR ($CDCl_3$/TFA): δ = 196.81 (C-1′), 192.31 (C-1″), 173.40 (C-2), 146.38, 144.27, 142.68 (C-3a, -9a, -10a), 140.09 (C-2″), 137.32 (C-6), 134.82, 132.64 (C-5″, -8), 129.62, 128.25 (C-3″, -4″), 127.21 (C-9), 118.24 (C-7), 112.59, 112.00 (C-1, -3), 30.08 (C-2′), 19.46 (CCH_3). – $C_{20}H_{15}N_3O_2$ (329.3): calcd. C 72.92, H 4.59, N 12.76; found C 73.08, H 4.62, N 12.86. – Mol. mass 329 (MS).

7-Benzoyl-8,9,10,11-tetrahydro-9,9-dimethylindeno[1,2-e]pyrido[1,2-b]-as-triazin-11-one (**11**): M.p. >250°C (DMF). Yield: 0.24 (65%). – IR (KBr): $\tilde{\nu}$ = 3100 cm^{-1}, 3080, 3060, 2950, 2890, 2860, 1630, 1610, 1600, 1570, 1560, 1510, 1470, 1440, 1400, 1330, 1290, 1270, 1200, 1170, 1140, 1120, 1090, 850, 790, 730, 720, 700, 660, 610. – UV (chloroform): λ_{max} (lg ε) = 254 nm (4.360), 290 (4.498), 368 (4.121), 398 (3.997), 506 (3.495). – ^{1}H NMR ($CDCl_3$/TFA): δ = 8.75 (m, 1H, 4-H, J_o = 7, J_m = 1.2 Hz), 8.32 (m, 1H, 1-H, J_o = 8.5, J_m = 1.5 Hz), 8.27 (m, 1H, 2-H, J_o = 8.5 and 7, J_m = 1.2 Hz), 7.77, 7.70, 7.55 (m, 5H, 3′-, 4′-, 5′-, 6′-, 7′-H), 7.75 (m, 1H, 3-H, J_o = 7 and 7, J_m = 1.5 Hz), 3.11 (s, 2H, 8-H), 2.68 (s, 2H, 10-H), 1.15 (s, 3H, CH_3). – ^{13}C NMR ($CDCl_3$/TFA): δ = 196.81, 192.31 (C-1′, -11), 177.13 (C-7a), 149.37, 144.38, 143.71 (C-6a, -12a, -11b), 138.50, 138.45, 133.76 (C-5′, -4, -2), 129.66 (C-4′), 128.69 (C-9), 126.87 (C-1), 121.38 (C-3), 117.47, 109.33 (C-11a, -7), 49.51 (C-10), 41.59 (C-8), 35.30 (C-9), 28.28 (CCH_3). – $C_{23}H_{19}N_3O_2 \cdot 1/2\ H_2O$ (378.4): calcd. C 72.99, H 5.33, N 11.10; found C 72.72, H 5.10, N 11.15. – Mol. mass 369 (MS).

2-(Dicyanomethylene)-3-phenacyl-2H-pyrido[1,2-b]-as-triazine (**12**): M.p. >250°C (acetonitrile/acetic acid). Yield: 0.15 (48%). – IR (KBr): $\tilde{\nu}$ = 3110 cm^{-1}, 2955, 2930, 2200, 2170, 1680, 1640, 1590, 1450, 1420, 1390, 1330, 1220, 1180, 1140, 990, 870, 770, 690, 580. – ^{1}H NMR ($CDCl_3$/[D_6]DMSO): δ = 8.11 (m, 1H, 6-H, J_o = 6.8, J_m = 1.5 Hz), 8.0, 7.52, 7.63, 8.32 (m, 5H, 4″-, 5″-, 6″-, 7″-, 8″-

H), 7.82 (m, 1H, 8-H, J_o = 8.6 and 7, J_m = 1.5 Hz), 7.45 (m, 1H, 9-H, J_o = 8.6, J_m = 1.8 Hz), 7.04 (m, 1H, 7-H, J_o = 7 and 6.8, J_m = 1.8 Hz), 4.38 (s, 2H, 1″-H). – ^{13}C NMR ($CDCl_3$/[D_6]DMSO): δ = 193.37 (C-2″), 155.01, 149.08, 146.08 (C-2, -3, -9a), 139.84 (C-6), 136.34, 133.04 (C-6″, -8), 138.65 (C-3″), 127.96, 127.58 (C-4″, -5″), 123.05 (C-9), 116.89, 115.63 (CN), 115.47 (C-7), 77.6 (C-1′), 44.25 (C-1″). – $C_{18}H_{11}N_5O$ (313.3): calcd. C 69.00, H 3.54, N 22.35; found C 69.08, H 3.70, N 22.53.

2-Amino-3-benzoylcyclopenta[e]pyrido[1,2-b]-as-triazine-1-carbonitrile (**13**): To a solution of compound **12** (0.31 g, 1.0 mmol) in anhydrous pyridine (6 ml) was added *p*-toluenesulfonic acid (0.05 g), and the mixture was heated at 100°C for 5 h. Upon cooling the product precipitated, it was filtered off and recrystallized from acetic acid. Yield: 0.22 g (71%), m.p. >250°C. – IR (KBr): $\tilde{\nu}$ = 3360 cm^{-1}, 3280, 3200, 3030, 2210, 1640, 1600, 1580, 1520, 1490, 1470, 1440, 1400, 1320, 1270, 1160, 1130, 690, 590, 530. – UV (acetonitrile): λ_{max} (lg ε) = 274 nm (4.451), 322 (4.561). – ^{1}H NMR ([D_6]DMSO): δ = 9.48, 9.02 (2 s, NH_2), 8.27 (m, 1H, 6-H, J_o = 6.6, J_m = 1.2 Hz), 8.04 (m, 1H, 8-H, J_o = 8.5 and 7, J_m = 1.2 Hz), 7.89 (m, 1H, 9-H, J_o = 8.5, J_m = 1.6 Hz), 7.78, 7.60, 7.51 (m, 5H, 3′-, 4′-, 5′-, 6′-, 7′-H), 7.43 (m, 1H, 7-H, J_o = 8.6 and 6.6, J_m = 1.2 Hz). – ^{13}C NMR ($CDCl_3$/[D_6]DMSO): δ = 188.03 (C-1′), 169.03 (C-2), 148.04, 145.06, 143.48 (C-3a, -9a, -10a), 140.31 (C-2′), 136.95, 135.68, 130.02 (C-5′, -8, -6), 128.03, 126.85 (C-3′, -4′), 124.26 (C-9), 117.19 (C-7), 114.15 (CN), 91.88 (C-3), 70.66 (C-1). – $C_{18}H_{11}N_5O$ (313.3): calcd. C 69.00, H 3.54, N 22.35; found C 69.26, H 3.62, N 22.53. – Mol. mass 313 (MS).

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[87/94]