Facile bromination of the benzene ring during the cyclisation of the 1*H*-3-methyl-4-ethoxycarbonyl-5--arylidenehydrazonopyrazoles to the 3-substituted-aryl-1*H*-6-methyl-7-ethoxycarbonyl--pyrazolo[3,2-*c*]-s-triazoles

Carol Csunderlik, Vasile Bercean*, Francisc Peter, and Valentin Badea

Department of Organic Chemistry and Technologies, 6 Bocşa Str, University "Politehnica" of Timisoara, 1900 Timişoara, Romania
E-mail: vbercean@mail.dnttm.ro

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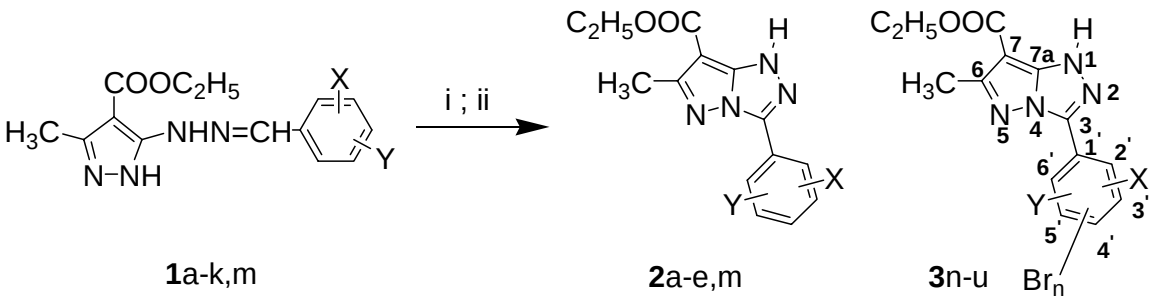
Abstract

1H-3-Substituted-aryl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-*c*]-s-triazoles **2**, **3** were obtained by the action of the bromine on the 1H-3-methyl-4-ethoxycarbonyl-5-aryllidenehydrazono-pyrazoles **1** and were transformed, after hydrolysis-decarboxylation to 1H-3-substituted-aryl pyrazolo[3,2-*c*]-s-triazoles **5** in the azomethyne dyes **6**.

Keywords: Bromination, hydrolysis-decarboxylation, 5-arylidenehydrazonopyrazoles, pyrazolo[3,2-*c*]-*s*-triazoles, azomethyne dyes

Introduction

3,6-Disubstituted pyrazolo[3,2-*c*]-s-triazoles were synthetised[1] and utilized for the preparation of couplers for photographic materials[2,3,4] and for their biological activitie[5]. 1H-3-Substituted-aryl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-c]-s-triazoles **2** were prepared by the action of the bromine in acetic acid in the presence of anhydrous sodium acetate[1] or by the action of lead tetraacetate in acetic acid[6] on the 1H-3-methyl-4-ethoxycarbonyl-5-arylidenehydrazono-pyrazole **1** (Scheme 1).



1a-k,m **2**a-e,m **3**n-u

i = Br_2 / CH_3COOH /CH_3COONa ii = $Pb(CH_3COO)_4$ / CH_3COOH
X=2-NO_2 Y=H b) X=4-NO_2 Y=H c) X=2-Cl Y=H d) X=4-CH_3 Y=H e) X=2OCH_3 Y=H f) X=2-OH Y=H g) X=4-OH Y=H h) X=3-OH Y=H i) X=2-OH Y=4-OH j) X=4-OCH_3 Y=H k)X=2-OCH_3 Y=4-OCH_3 m) X=4-OH Y=3,5-(t-C_4H_9)$_2$ n) X=2-OCH_3 Y=H Br_n=(3)5-Br o) X=2-OH Y=H Br_n=3,5-Br_2 p) X=4-OH Y=H Br_n=3,5-Br_2 r) X=3-OH Y=H Br_n=2,4,6-Br_3 s) X=2-OH Y=4-OH Br_n=3,5-Br_2 t) X=4-OCH_3 Y=H Br_n=3-Br u) X=2-OCH_3 Y=4-OCH_3 Br_n=5-Br

Scheme 1

Results and Discussion

The bromine action on the 1H-3-methyl-4-ethoxycarbonyl-5-aryllidenehydrazono-pyrazole **1** in acetic acid in the presence of anhydrous sodium acetate led mainly to the pyrazolo-triazole **2**a-e in the case of the substituents X=2-NO_2 **1**a[1], 4-NO_2 **1**b[1], 2-Cl **1**c[1], 4-CH_3 **1**d[1] or p-$N(CH_3)_2$[7] and 2-OCH_3 **1**e.[7] In the case of the electron donating groups (OH, OCH_3) and utilization of excess of the bromine in the presence of a calculated excess of anhydrous sodium acetate, the obtained pyrazolo triazoles **3**n-u are brominated at the benzene ring. The bromination occurs mainly at the activated free positions. In the case of the hydroxy groups, all the activated free positions, related to the hydroxy groups are substituted, but in the case of methoxy groups, only one position is occupied. If the activated positions are not free (**1**m X=4-OH, Y=3,5-tBu_2) the action of the bromine led to pyrazolo-triazole **2**m.

In the case of compound **1**e the action of one equivalent of the bromine led to **2**e[7] whereas the action of two equivalent of the bromine led to **3**n and a little quantity of **2**e. The two molecular peaks M^+(m/z) at 378, 380 confirm monobromination.

Differently, the action of one equivalent of the bromine on the **1**j afford to a mixture of **1**j **2**j and **3**t whereas two equivalent of the bromine led to **3**t and a little quantity of **2**j. The two molecular peaks M^+ (m/z) at 378, 380 confirm monobromination and ^{1}H-NMR and ^{13}C-NMR spectra proved the structure of the **3**t.

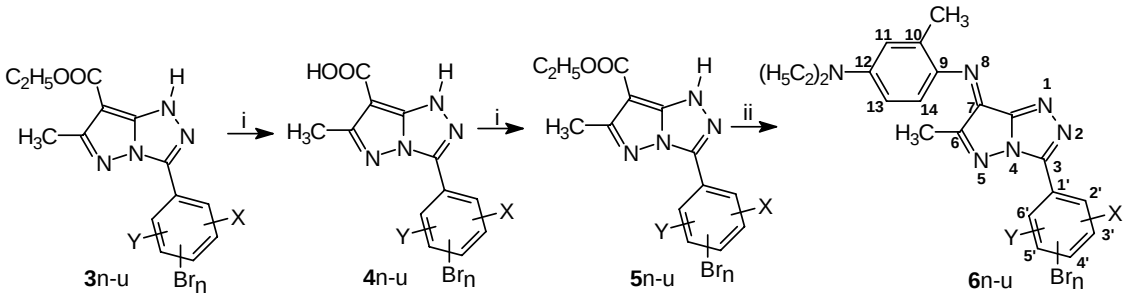
Also by the action of one equivalent of the bromine on the **1**k, a mixture of **1**k **2**k and **3**u was formed, whereas two equivalent of the bromine led to **3**u. The two molecular peaks M^+ (m/z) at

408, 410 confirmed the monobromination and ^{1}H-NMR and ^{13}C-NMR spectra proved the structure of the **3**u.

In the case of the compounds **1**f-i, which contains hydroxy groups, utilization of one equivalent of the bromine led to a mixture of compounds. Use of tree equivalents of the bromine for **1**f **1**g **1**i led to the dibrominated compounds **3**o **3**p **3**s whereas the utilization of four equivalents of the bromine for **1**h led to the tribrominated compound **3**r. The dibromination was confirmed by the tree molecular peaks M^{+}(m/z) at 442, 444, 446 for **3**o, M^{+}(m/z) at 442, 444, 446 for **3**p, M^{+}(m/z) at 458, 460, 462 for **3**s, and the tribromination by the four molecular peaks M^{+}(m/z) at 520, 522, 524, 526 for **3**r. The structures of the compounds **3**o-s were confirmed also by ^{1}H-NMR and ^{13}C-NMR spectra.

The formation and the structure of compounds **3**n-u were also confirmed by the synthesis and characterization of compounds **5**n-u and of their azomethynic dyes **6**n-u. (Scheme2). The ethoxycarbonyl groups from the 3-substituted aryl-1H-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-*c*]-s-triazoles **3**n-u were eliminated by hydrolysis and decarboxylation to the 3-substituted aryl-1H-6-methyl-pyrazolo[3,2-*c*]-s-triazoles **5** which were converted to the azomethine dyes **6** by coupling with 2-methyl-4-N,N-
-diethylamino-aniline **7** in aqueous-alkaline $K_3Fe(CN)_6$ solution (Scheme 2).

Our preliminary experiments on the hydrolysis of the compounds **3**n-u by heating them 30min at 100 °C with concentrated H_2SO_4, showed that the acids **4**n-u contained variable amounts of the decarboxylated compounds **5**n-u and in some cases, the starting material, the esters **3**.



i= H_2SO_4 80% / CH_3COOH 4-6 h reflux ii=2,4-$(CH_3)(NEt_2)C_6H_3NH_2$ **7** / $K_3Fe(CN)_6$ /NH_4OH-C_2H_5OH

Scheme 2

This facile decarboxylation of the compounds **4** to **5** during the hydrolysis with concentrated H_2SO_4 determined us to try one-pot hydrolysis-decarboxylation of **3**n-u to **5**n-u by 4-6 hours of refluxing with a solution of 80% H_2SO_4 in acetic acid, method utilized by us for the previously described hydrolysis-decarboxylation of the compounds **2**.[7] The new compounds **5**n-u were

characterized by melting point, mass spectrometry, which confirmed the degree of brominating, IR, ^{1}H-NMR and ^{13}C-NMR spectroscopy. They were also characterized by coupling with 2-methyl-4-N,N-diethylamino-aniline **7** in the presence of potassium fericyanide in ethanol-ammonium hydroxide solution. The new azomethyne dyes **6** were characterized by mass spectrometry, UV–VIS, ^{1}H-NMR and ^{13}C-NMR spectroscopy. The preparation of the compounds **5**t **6**t and **6**s were unsuccessful. A single alkaline-hydrolysis experiment of the compound **3**f to **4**f was successful and after the extension of the experiment to all the compounds **3** it will be reported.

Experimental Section

General Procedures. TLC was performed using aluminium plates precoated with silica gel 60 or 60 F_{254} (Merck) and visualized by iodine or UV light (254 nm). Melting points were determined on a Böetius PHMK (Veb Analytik Dresden) apparatus. The NMR spectra were recorded on a Varian Gemini 300 and Bruker DRX 400 spectrometer at 25 ºC, unless otherwise stated. ^{1}H- and ^{13}C-NMR signals were referenced to TMS and the solvent shift ($(CD_3)_2SO$ δ_H 2.50 and δ_C 39.5). Coupling constants are given in Hz and without sign. The IR-spectra were recorded (KBr) on a Jasco FT/IR-410 instrument; the UV–VIS spectra were recorded (CH_3OH) on a M40 Karl Zeiss Jena instrument. Mass spectrometry was carried out on a Varian FINNIGAN MAT 212 instrument and the elementar analysis on the Perkin Elmer 240 instrument.

Materials. 1H-3-methyl-4-ethoxycarbonyl-5-aryllidene-hydrazono-pyrazoles **1**e-k,m were obtained according to the literature.[1,7] The others materials were commercial samples. All organic solvents were of analytical quality and used as purchased. Solvent mixtures are defined by volume ratios (v/v).

1*H*-3-Substituted aryl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-c]-s-triazoles 3n-u

To a solution of 5 mmol 1H-3-methyl-4-ethoxycarbonyl-5-aryllidenehydrazono-pyrazole **1** e-k, m in 15-25 mL acetic acid was added

10 mmol anhydrous sodium acetate for the compounds **1**m

20 mmol anhydrous sodium acetate for the compounds **1**e, j, k

30 mmol anhydrous sodium acetate for the compounds **1**f, g, i and

40 mmol anhydrous sodium acetate for the compounds **1**h

After dissolution by heating of the anhydrous sodium acetate, the solution was cooled to room temperature (water bath) and a solution of

5 mmol Br_2 in 5 mL solution of acetic acid for the compounds **1**m

10 mmol Br_2 in 10 mL solution of acetic acid for the compounds **1**e, j, k

15 mmol Br_2 in 15 mL solution of acetic acid for the compounds **1**f, g, i and

20 mmol Br_2 in 20 mL solution of acetic acid for the compounds **1**h

was dropped during 10-15 minutes. The formed solution (suspension) was stirred to room temperature for 30 minutes and 1 hour to 100 °C (water bath). After cooling to room temperature, the suspensions were filtered to afford the compounds **3**n,o,r-u or the solutions were precipitated in water to afford the compounds **2**m **3** p.

1*H*-3-(5-Bromo-2-methoxy)-phenyl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-c]-s-triazole (3n). White powder (yield 78%); mp186-188 °C (acetic acid); MS m/z: 378, 380(M+): IR ν 3227, 3077, 3037, 2978, 2929, 2909, 2843, 1715, 1627, 1596, 1501, 1275, 1217, 1159, 1098, 1014, 879, 808, 771, 727, 689, 621 cm^{-1}; Anal. Calcd for $C_{15}H_{15}BrN_4O_3$: C,47.51; H,3.99; N, 14.77; Found: C,47.43; H,4.05; N,14.74.

1*H*-3-(3,5-Dibromo-2-hydroxy)-phenyl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-c]-s-triazoles (3o). White powder (yield 88%); mp300-302 °C (acetic acid); MS m/z: 442, 444, 446 (M+); IR ν 3190, 3071, 2990, 2971, 1655, 1626, 1322, 1258, 1233, 1187, 1178, 1094, 1045, 1018, 645, 604 cm^{-1}; ^{1}H-NMR δ 10.61 (1H, bs, NH), 8.58 (1H, d, *J*=2.0, 6´-H), 8.01 (1H, d, *J*=2.0, 4´-H), 4.34 (2H, q, *J*=7.1, CH_3-*CH_2*-O), 3.35 (1H, bs, OH), 2.60 (3H, s, CH_3-6-C), 1.42 (3H, t, *J*=7.1, *CH_3*-CH_2-O); ^{13}C-NMR δ 162.99 (C=O), 160.83 (2´-C), 152.73 (7a-C), 148.79 (6-C), 137.35 (4´-C), 129.54 (6´-C), 114.02 (1´-C), 112.92 (5´-C), 112.03 (3´-C), 88.71 (7-C), 59.83 (CH_3-*CH_2*-O), 15.22 (*CH_3*-CH_2-O), 14.85 (CH_3-6-C), (Bruker DPX 300); Anal. Calcd for $C_{14}H_{12}Br_2N_4O_3$: C,37.86; H,2.72; N, 12.62; Found: C,37.81; H,2.81; N,12.64.

1*H*-3-(3,5-Dibromo-4-hydroxy)-phenyl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-c]-s-triazole (3p). Faintly violet powder (yield 84%); mp 213-215°C (ethanol); MS m/z: 442, 444, 446 (M+); IR ν 3470, 3256, 3078, 2980, 2932, 1702, 1658, 1621, 1326, 1232, 1172, 1103, 1022, 685, 652, 583 cm^{-1}; ^{1}H-NMR δ 10.58 (1H, bs, NH), 8.11 (2H, s, 2´-H, 6´-H), 8.00 (1H, bs, OH), 4.23 (2H, q, *J*=7.1, CH_3-*CH_2*-O), 2.28 (3H, s, CH_3-6-C), 1.30 (3H, t, *J*=7.1, *CH_3*-CH_2-O); ^{13}C-NMR δ 159.00 (7a-C), 161.43 (C=O), 151.00 (3-C), 137.00 (6-C), 129.46 (2´-C, 6´-C), 122.50 (1´-C), 112.17 (3´-C, 5´-C), 82.5 (7-C), 59.08 (CH_3-*CH_2*-O), 14.51 (*CH_3*-CH_2-O), 14.37 (CH_3-6-C); Anal. Calcd. for $C_{14}H_{12}Br_2N_4O_3$: C,37.86; H,2.72; N, 12.62; Found: C,37.83; H,2.85; N,12.57.

1*H*-3-(3,5-Dibromo-2,4-dihydroxy)-phenyl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-c]-s-triazole (3s). Faintly brown powder (yield 75%); mp 302-305 °C (ethanol); MS m/z:458, 460, 462(M+);IR ν 3493, 3263, 3188, 2988, 2935, 1651, 1616, 1322, 1213, 1174, 1105, 1026, 698, 657, 605 cm^{-1}; ^{13}C-NMR δ 161.74 (C=O), 159.47 (4´-C), 153.50 (2´-C), 152.95 (7a-C), 146.68 (6-C), 136.56 (3-C), 128.71 (6´-C), 118.77 (1´-C), 104.37 (5´-C), 101.11 (3´-C), 86.75 (7-C), 59.09 (CH_3-*CH_2*-O), 14.33 (*CH_3*-CH_2-O), 14.32 (CH_3-6-C), (Bruker AC 200); Anal. Calcd. for $C_{14}H_{12}Br_2N_4O_4$: C,36.55; H,2.63; N, 12.18; Found: C,36.53; H,2.72; N,12.09.

1*H*-3-(5-Bromo-2,4-dimethoxy)-phenyl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-c]-s-triazole (3u). White powder (yield 60%); mp 222-224°C (ethanol); MS m/z:408, 410(M+); IR ν 3430, 3151, 2978, 2938, 2845, 1700, 1619, 1605, 1506, 1369,1277, 1210, 1160, 1096, 1021, 693, 570, 547 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 7.75 (1H, s, 6´-H), 6.82 (1H, s, 3´-H), 4.30 (2H, q, *J*=7.1, CH_3-*CH_2*-O), 3.95 (3H, s, CH_3-O), 3.88 (3H, s, CH_3-O), 2.32 (3H, s, CH_3-6-C), 1.29 (3H, t, *J*=7.1, *CH_3*-CH_2-O); ^{13}C-NMR δ 162.63(C=O), 161.54 (4´-C), 158.45 (2´-C), 153.02 (3-C),

151.90 (7a-C), 148.15 (6-C), 132.05 (6´-C), 131.89 (3´-C), 113.60 (1´-C), 100.75 (5´-C), 88.65 (7-C), 59.61 (CH_3-*CH_2*-O), 56.92 (CH_3O), 56.25 (CH_3O), 15.31 (CH_3-*CH_2*-O), 13.10 (CH_3-6-C); Anal. Calcd. for $C_{16}H_{17}BrN_4O_4$: C,46.96; H,4.19; N, 13.69; Found: C,46.91; H,4.25; N,13.59.

1*H*-3-(3-Bromo-4-methoxy)-phenyl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-c]-s-triazole (3t). Faintly gray powder (yield 80%); mp 196-198 °C (acetic acid); MS m/z: 378, 380(M+);IR ν 3209, 3000, 2972, 2933, 2833, 1649, 1626, 1504, 1321, 1252, 1175, 1098, 1021,1001, 739, 609, 520 cm^{-1}; ^{1}H-NMR δ 13.90 (1H, s, NH), 8.48 (1H, d, *J*=2.0, 2´-H), 8.27 (1H, dd, *J*=8.8, 2.0, 6´-H), 7.33 (1H, d, *J*=8.8, 5´-H), 4.24 (2H, q, *J*=7.1, CH_3-*CH_2*-O), 3.95 (3H, s, CH_3O), 2.58 (3H, s, CH_3-6-C), 1.33 (3H, t, *J*=7.1, *CH_3*-CH_2-O); ^{13}C-NMR δ 162.06 (C=O), 159.15 (4´-C), 156.80 (7a-C), 147.89 (3-C), 137.05 (6-C), 130.00 (2´-C), 126.85 (6´-C), 118.84 (1´-C), 113.04 (5´-C), 111.01 (3´-C), 86.67 (7-C), 59.02 (CH_3-*CH_2*-O), 56.47 (CH_3-O), 14.48 (*CH_3*-CH_2-O), 13.52 (CH_3-6-C); Anal. Calcd. for $C_{15}H_{15}BrN_4O_3$: C,47.51; H,3.99; N, 14.77; Found: C,47.48; H,4.06; N,14.69.

A small amount of the isomeric 1H-3-(2-bromo-4-methoxy)-phenyl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-c]-s-triazole was evidenced in the 400MHz spectra.

1*H*-3-(3-Hydroxy-2,4,6-tribromo)-phenyl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-c]-s-triazole (3r). White powder (yield 50%); MS m/z: 520, 522, 524, 526(M+); IR ν 3497, 3173, 3074, 3005, 2940, 1660, 1616, 1328, 1223, 1181, 1117, 1094, 1016, 688, 672, 592 cm^{-1}; ^{1}H-NMR δ 10.78 (1H, bs, NH), 8.10 (1H, s, 5´-H), 3.38 (1H, bs, OH), 2.72 (2H, q, *J*=7.1, CH_3-*CH_2*-O), 2.42 (3H, s, *CH_3*-6-C), 1.28 (3H, t, *J*=7.1, *CH_3*-CH_2-O) ; ^{13}C-NMR δ 161.96 (C=O), 159.28 (3´-C), 151.54 (7a-C), 147.11 (3-C), 137.60 (6-C), 134.94 (5´-C), 127.49 (1´-C), 116.21 (6´-C), 116.17 (4´-C), 114.49 (2´-C), 87.00 (7-C), 59.14 (CH_3-*CH_2*-O), 14.55 *CH_3*-6-C), 14.55 (*CH_3*-CH_2-O). (Bruker AC 200); Anal. Calcd. for $C_{14}H_{11}Br_3N_4O_3$: C,32.15; H,2.12; N, 10.71; Found: C,32.13; H,2.17; N,10.69.

1*H*-3-(4-Hydroxy-3,5-di-t-butyl)-phenyl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-c]-s-triazole (2m). Faintly yellow powder (yield 95%); mp253-256 °C (benzene–petr. et.); MS m/z:398(M+); IR ν 3605, 3447, 3144, 2958, 2909, 2874, 1713, 1669, 1622, 1319, 1240, 1223, 1198, 1159, 1099, 1024 cm^{-1}; ^{1}H-NMR δ 13.69 (1H, s, NH), 9.83 (1H, s, OH), 8.21 (2H, s, 2´-H, 6´-H), 4.30 (2H, q, *J*=7.1, CH_3-*CH_2*-O), 2.50 (3H, s, *CH_3*-6-C), 1.46 (18H, s, t-Bu), 1.33 (3H, t, *J*=7.1, *CH_3*-CH_2-O); ^{13}C-NMR δ 162.21 (C=O), 158.78 (7a-C), 156,00 (3-C), 147.94 (4´-C), 139.39 (3´-C), 139.36 (6-C), 122.92 (6´-C), 116.60 (1´-C), 86.41 (7-C), 58.96 (CH_3-*CH_2*-O), 34.69 (*C*-Me_3), 30.04 (C-*Me_3*), 14.80 (*CH_3*-CH_2-O), 14.50 (*CH_3*-6-C).

A small amount (up to 5%) of the 1H-3-(3-bromo-4-hydroxy-5-t-butyl)-phenyl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-c]-s-triazole was evidenced in the 400 MHz spectra.

1*H*-3-Substituted aryl-6-methyl-pyrazolo[3,2-c]-s-triazoles (5n-u)

A mixture of 1mmol 1H-3-substituted aryl-6-methyl-7-ethoxycarbonyl-pyrazolo[3,2-c]-s-triazoles **3**n-u in 8 mL acetic acid and 2mL H_2SO_4 80% was refluxed for 4-7 h (TLC benzene / ethyl acetate 1:1). The reaction mixture was filtered, the solution precipitated in 50 mL water, neutralized with 10% NaOH solution, the suspension filtered and the products **5**n-u recrystallised.

Preparation of the azomethyne dyes: 3-Substituted-phenyl-6-methyl-7-(2-methyl-4-diethylamino-phenyl-imino-pyrazolo-[3,2-c]-s-triazoles 6n-u

To a solution of 1mmol of the compounds **5**n-u and 1,1 mmol **7** in 15-20 mL ethanol was dropped with stirring a solution of 4,4 mmol $K_3Fe(CN)_6$ in 10 mL water and 2 mL 25% ammonium hydroxide. After 10 minute stirring to room temperature the reaction mixture was poured into 100 mL water and filtered. The compounds **6**n-u were recrystallised from $CH_3COOC_2H_5$–petroleum ether.

1*H*-3-(5-Bromo-2-methoxy)-phenyl-6-methyl-pyrazolo[3,2-c]-s-triazole (5n). White powder (yield 59%); MS m/z: 306, 308(M+); IR ν 3429, 3220, 3155, 3105, 3074, 3021, 2968, 2928, 2897, 2838, 1611, 1506, 1261, 1185, 1085, 1020, 695, 630, 563, 546 cm^{-1}; ^{1}H-NMR ($CDCl_3$ with CF_3COOH) δ 7.87 (1H, d, *J*=2.50, 6´-H), 7.33 (1H, dd, *J*=2.50, *J*=9.0, 4´-H), 7.03 (1H, d, *J*=9.0, 3´-H), 6.27 (1H, bs, 7-H), 3.95 (3H, s, OCH_3), 2.55 (3H, s, CH_3-6-C); ^{13}C-NMR δ 161.65 (2´-C), 156.35 (7a-C), 154.50 (3-C), 148.12 (6-C), 137.49 (4´-C), 133.03 (6´-C), 120.21 (1´-C), 114.14 (3´-C), 108.88 (5´-C), 82.26 (7-C), 57.00 (CH_3O-2´C), 12.64 (CH_3-6C); Anal. Calcd. for $C_{12}H_{11}BrN_4O$: C,46.93; H,3.61; N, 18.24; Found: C,46.89; H,3.70; N,18.27.

6n. MS m/z: 480, 482(M+); λ_{max}: 558nm(ε 5,9x10^4); ^{1}H-NMR ($CDCl_3$) δ 9.22 (1H, d, *J*=9,50, 14-H), 7.96 (1H, d, *J*=2.50, 6´-H), 7.55 (1H, dd, *J*=2.50, *J*=8.90, 4´-H), 6.93 (1H, d, *J*=8.90, 3´-H), 6.79 (1H, dd, *J*=3.00, *J*=9.50, 13-H), 6.63 (1H, d, *J*=3.00, 11-H), 3.89 (3H, s, OCH_3), 3.51 (4H, q, *J*=7.10, -N-*CH_2*-CH_3), 2.57 (3H, s, *CH_3*-6-C), 2.49 (3H, s, CH_3-10-C), 1.27 (6H, t, *J*=7.10, N-CH_2-*CH_3*); ^{13}C-NMR δ 168.09 (7-C), 156.94 (2´-C), 153.00 (3-C), 151.62 (7a-C), 148.59 (6-C), 146.19 (12-C), 142.20 (9-C), 135.20 (10-C), 134.34 (4´-C), 133.74 (6´-C), 127.05 (14-C), 116.75 (1´-C), 113.59 (3´-C), 112.80 (5´-C), 112.57 (11-C), 110.40 (13-C), 56.28 (CH_3O-), 45.01 (CH_3-*CH_2*-N), 19.45 (*CH_3*-10-C), 12.88 (*CH_3*-CH_2-N), 12.66 (*CH_3*-6-C); Anal. Calcd. for $C_{23}H_{25}BrN_6O$: C,57.39; H,5.23; N, 17.46; Found: C,57.32; H,5.28; N,17.39.

1*H*-3-(3,5-Dibromo-2-hydroxy)-phenyl-6-methyl-pyrazolo[3,2-c]-s-triazole (5o). White powder (yield 90%); mp235-237 °C (ethanol–water); MS m/z: 370, 372, 374(M+); IR ν 3595, 3407, 3143, 3075, 2976, 2927, 1607, 1237, 1188, 1103, 1032, 647, 618, 556cm^{-1}; ^{1}H-NMR ($CDCl_3$ with CF_3COOH) δ 7.92 (1H, d, *J*=2.50, 6´-H), 7.89 (1H, d, *J*=2.50, 4´-H), 6.29 (1H, s, 7-H), 2.57 (3H, s, CH_3-6-C); ^{13}C-NMR δ 161.48 (2´-C), 155.10 (7a-C), 149.05 (6-C), 148.31 (3-C), 138.82 (4´-C), 131.60 (6´-C), 119.80 (1´-C), 114.38 (5´-C), 108.49 (3´-C), 86.05 (7-C), 12.30 (CH_3-6-C); Anal. Calcd. for $C_{11}H_8Br_2N_4O$: C,35.51; H,2.17; N, 15.06; Found: C,35.49; H,2.22; N,15.02.

6o. MS m/z: 544, 546, 548(M+); λ_{max}: 576nm(ε 7,9x10^4); ^{1}H-NMR ($CDCl_3$) δ 9.10 (1H, d, *J*=9.35, 14-H), 8.51 (1H, d, *J*=2.35, 6´-H), 7.76 (1H, d, *J*=2.35, 4´-H), 6.82 (1H, dd, *J*=9.35, *J*=2.90, 13-H), 6.62 (1H, d, *J*=2.90, 11-H), 3.51 (4H, q, N-*CH_2*-CH_3), 2.57 (3H, s, CH_3-6-C), 1.29 (6H, t, *J*=7.10, N-CH_2-*CH_3*); ^{13}C-NMR δ 167.90 (7-C), 160.00 (2´-C), 152.82 (3-C), 149.30 (7a-C), 148.20 (6-C), 144.63 (12-C), 141.03 (9-C), 137.02 (4´-C), 135.80 (10-C), 128.49 (6´-C), 127.57 (14-C), 119.10(1´-C), 113.18 (13-C), 112.20 (11-C), 111.30 (5´-C), 111.05 (3´-C), 45.67 (CH_3-*CH_2*-N), 19.92 (*CH_3*-10-C), 13.41 (*CH_3*-CH_2-N), 13.27 (*CH_3*-6-C); Anal. Calcd. for $C_{22}H_{22}Br_2N_6O$: C,48.37; H,4.06; N, 15.38; Found: C,48.39; H,4.12; N,15.33.

1*H*-3-(3,5-Dibromo-4-hydroxy)-phenyl-6-methyl-pyrazolo[3,2-c]-s-triazole (5p). Brown powder (yield 41%); MS m/z: 370, 372, 374(M+); IR ν 3612, 3488, 3381, 3142, 3078, 2990, 2923, 1601, 1243, 1163, 1095, 1041,1000, 678, 621,558 cm^{-1}; ^{1}H-NMR ($CDCl_3$ with CF_3COOH) δ 8.02 (2H, s, 2′, 6′-H), 6.26 (1H, s, 7-H), 2.56 (3H, s, CH_3-6-C);
^{13}C-NMR δ 162.10 (4′-C), 156.50 (7a-C), 153.30 (3-C), 149.10 (6-C), 130.67 (2′-C, 6′-C), 120.31 (1′-C), 108.99 (3′-C, 5′-C), 86.81 (7-C), 12.67 (CH_3-6-C); Anal. Calcd. for $C_{11}H_8Br_2N_4O$: C, 35.51; H, 2.17; N, 15.06; Found: C,35.47; H,2.25; N,15.01.
6p. MS m/z: 544, 546, 548(M+); λ_{max}: 572nm(ε 3,5x10^4); ^{1}H-NMR ($CDCl_3$) δ 8.98 (1H, d, *J*=9.30, 14-H), 7.84 (2H, s, 2′, 6′-H), 6.83 (1H, dd, *J*=9.30, *J*=2.90, 13-H), 6.60 (1H, d. *J*=2.90, 11-H), 3.51 (4H, q, *J*=7.10, N-*CH_2*-CH_3), 2.55 (3H, s, CH_3-6-C), 2.53 (3H, s, CH_3-10-C), 1.28 (6H, t, *J*=7.10, N-CH_2-*CH_3*); ^{13}C-NMR δ 165.85 (7-C), 163.20 (4′-C), 152.80 (3-C), 151.60 (7a-C), 148.70 (6-C), 146.50 (12-C), 142.31 (9-C), 134.93 (10-C), 130.82 (2′-C, 6′-C), 126.80 (14-C), 119.50 (1′-C), 112.80 (11-C), 111.85 (3′-C, 5′-C), 109.85 (13′-C), 45.10 (CH_3-*CH_2*-N), 19.40 (*CH_3*-10-C), 12.81 (*CH_3*-CH_2-N), 12.65 (*CH_3*-6-C); Anal. Calcd. for $C_{22}H_{22}Br_2N_6O$: C, 48.37; H, 4.06; N, 15.38; Found: C,48.32; H,4.12; N,15.33.
1*H*-3-(3-Hydroxy-2,4,6-tribromo)-phenyl-6-methyl-pyrazolo[3,2-c]-s-triazole (5r). White-pink powder (yield 40%); MS m/z: 448, 450, 452, 454(M+); IR ν 3556, 3320, 3159, 3074, 2980, 2928, 1599, 1335, 1225, 1176, 1099,1065, 1014, 684, 656, 585 cm^{-1}; ^{1}H-NMR ($CDCl_3$ with CF_3COOH) δ 7.90 (1H, s, 5′-H), 6.27 (1H, s, 7-H), 2.56 (3H, s, CH_3-6-C); ^{13}C-NMR δ 164.10 (3′-C), 155.37 (7a-C), 150.77 (3-C), 147.64 (6-C), 135.81 (5′-C), 124.01 (1′-C), 120.20 (6′-C), 115.31 (4′-C), 108.87 (2′-C), 85.90 (7-C), 12.81 (CH_3-6-C); Anal. Calcd. for $C_{11}H_7Br_3N_4O$: C, 29.30; H, 1.56; N, 12.43; Found: C,29.25; H,1.60; N,12.36.
6r. MS m/z: 622, 624, 626, 628 (M+); λ_{max}: 553nm(ε 4,8x10^4); ^{1}H-NMR ($CDCl_3$) δ 9.05 (1H, d, *J*=9.30, 14-H), 8.15 (1H, s, 5′-H), 6.78 (1H, dd, *J*=9.30, *J*=2.90, 13-H), 6.56 (1H, d, *J*=2.90, 11-H), 3.50 (4H, q, *J*=7.10, N-*CH_2*-CH_3), 2.55 (3H, s, CH_3-6-C), 1.27 (6H, t, *J*=7.10, N-CH_2-*CH_3*); ^{13}C-NMR δ 164.25 (7-C), 163.10 (3′-C), 153.05 (3-C), 148.95 (7a-C), 148.35 (6-C), 144.52 (12-C), 143.50 (1′-C), 141.10 (9-C), 136.25 (5′-C), 135.76 (10-C), 127.60 (14-C), 118.76 (6′-C), 113.20 (13-C), 112.20 (11-C), 111.75 (4′-C), 110.20 (2′-C), 45.52 (CH_3-*CH_2*-N), 19.85 (*CH_3*-10-C), 13.45 (*CH_3*-CH_2-N), 13.25 (*CH_3*-6-C); Anal. Calcd. for $C_{22}H_{21}Br_3N_6O$: C, 42.27; H, 1.39; N, 13.44; Found: C,42.21; H,1.45; N,13.37.
1*H*-3-(3,5-Dibromo-2,4-dihydroxy)-phenyl-6-methyl-pyrazolo[3,2-c]-s-triazole (5s). Black powder (yield 76%); mp 145-147 °C (ethanol–water); MS m/z: 386, 388, 390 (M+); IR ν 3585, 3350, 3140, 3073, 2993, 2927,1605, 1324, 1212, 1100, 1018, 695, 647, 551 cm^{-1}; ^{1}H-NMR ($CDCl_3$ with CF_3COOH) δ 7.67 (1H, s, 6′-H), 6.31 (1H, s, 7-H), 2.55 (3H, s, CH_3-6-C); ^{13}C-NMR δ 167.62 (4′-C), 161.50 (2′-C), 156.42 (7a-H), 154.82 (3-C), 146.20 (6-C), 135.43 (6′-C), 115.32 (1′-C), 106.77 (5′-C), 101.20 (3′-C), 87.21 (7-C), 13.24 (*CH_3*-6-C); Anal. Calcd. for $C_{11}H_8Br_2N_4O_2$: C, 34.05; H, 2.08; N, 14.44; Found: C,34.00; H,2.12; N,14.39.
1*H*-3-(5-Bromo-2,4-dimethoxy)-phenyl-6-methyl-pyrazolo[3,2-c]-s-triazole (5u). Grey powder (yield 83%); mp 240-242 °C (ethanol); MS m/z: 336, 338(M+); IR ν 3368, 3061, 2941, 2838, 2749, 1605, 1280, 1213, 1173, 1092, 1017, 550 cm^{-1}; ^{1}H-NMR δ 7.26 (1H, s, 6′-H), 6.61

(1H, s, 3´-H), 5.56 (1H, s, 7-H), 3.98 (3H, s, CH_3-O), 3.91 (3H, s, CH_3-O), 2.43 (3H, s, CH_3-6-C); ^{13}C-NMR δ 162.00 (4´-C), 157.00 (2´-C), 156.50 (7a-C), 132.54 (6´-C), 132.50 (3´-C), 108.50 (1´-C), 98.28 (5´-C), 76.57 (7-C), 56.33 (CH_3O), 56.32 (CH_3O), 14.58 (CH_3-6-C) (Bruker DPX 300); Anal. Calcd. for $C_{13}H_{13}BrN_4O_2$: C, 46.31; H, 3.89; N, 16.62; Found: C,46.27; H,3.96; N,16.58.

6u. MS m/z: 510, 512(M+); λ_{max} 576 nm; ^{1}H-NMR ($CDCl_3$) δ 9.08 (1H, d, *J*=9.35, 14-H), 7.32 (1H, s, 6´-H), 6.90 (1H, dd, *J*=9.30, *J*=2.90, 13-H), 6.72 (1H, s, 3´-H), 6.57 (1H, d, *J*=2.90, 11-H), 3.98 (3H, s, CH_3-O), 3.51 (4H, q, *J*=7.10, N-*CH_2*-CH_3), 2.53 (3H, s, CH_3-10-C), 2.43 (3H, s, CH_3-6-C), 1,28 (6H, t, *J*=7.10, N-CH_2-*CH_3*); ^{13}C-NMR δ 163.25 (7-C), 162.85 (4´-C), 157.43 (2´-C), 152.23 (3-C), 151.94 (7a-C), 148.22 (6-C), 146.73 (12-C), 142.11 (9-C), 135.22 (10-C), 132.68 (6´-C), 132.33 (3´-C), 125.47 (14-C), 112.63 (1´-C), 111.81 (11-C), 109.90 (13-C), 99.19 (5´-C), 57.05 (CH_3O), 56.32 (CH_3O), 45.14 (CH_3-*CH_2*-N), 19.36 (*CH_3*-10-C), 13.90 (*CH_3*-CH_2-N), 13.21 (*CH_3*-6-C); Anal. Calcd. for $C_{24}H_{27}BrN_6O_2$: C, 56.36; H, 5.32; N, 16.43; Found: C,56.31; H,5.38; N,16.38 Anal. Calcd. for $C_{24}H_{27}BrN_6O_2$: C, 56.36; H, 5.32; N, 16.43; Found: C,56.31; H,5.38; N,16.38.

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