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LETTERS TO THE EDITOR

SYNTHESIS AND ELECTROPHILIC SUBSTITUTION OF DIPYRROLO-[1,2-*b*:3,4-*d*]PYRIDAZINES

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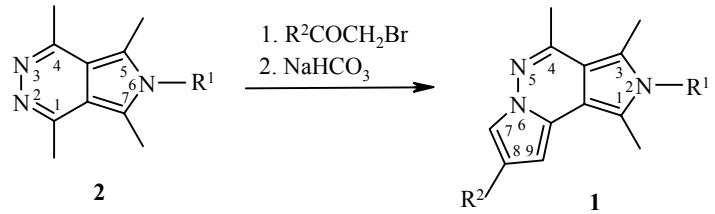
The synthesis and study of the properties of aza analogs of indolizines is a current area of investigation in the search for new physiologically active compounds [1]. We have synthesized a previously unknown tricyclic system, namely, dipyrrolo[1,2-*b*:3,4-*d*]pyridazine (**1**) from 1,4,5,7-tetramethyl-6-R^1-pyrrolo[3,4-*d*]-pyridazines (**2**), (obtained from the corresponding 3,4-diacetyl-2,5-dimethyl-1-R^1-pyrroles [2] and hydrazine hydrate in DMF) and α-bromo ketones with subsequent treatment of the reaction mixture by $NaHCO_3$ (Chichibabin method).



2 **1**

Fraser et al. [3, 4] have already used the Chichibabin reaction with pyridazines in the synthesis of pyrrolo[1,2-*b*]pyridazines.

Pyridazine **1** was found to have high nucleophlicity and electrophilic substitution occurs at $C_{(7)}$ or $C_{(7)}$ and $C_{(9)}$ depending on the steric bulk and activity of the attacking electrophile. We obtained products of diacetylation, diformylation, and azocoupling, namely, 7,9-diacetyl-1,3,4-trimethyl-8-phenyl-2-(4-tolyl)-dipyrrolo[1,2-*b*:3,4-*d*]pyridazine (**3**), 7,9-diformyl-1,2,3,4-tetramethyl-8-phenyldipyrrolo[1,2-*b*:3,4-*d*]-pyridazine (**4**), and 7-(4-methoxyphenylazo)-2-(4-tolyl)-1,3,4-trimethyl-8-phenyldipyrrolo[1,2-*b*:3,4-*d*]-pyridazine (**5**).

The ^1H NMR spectra were taken on a Bruker DPX-250 spectrometer at 250 MHz.

2-R^1-8-R^2-1,3,4-Trimethyldipyrrolo[1,2-*b*:3,4-*d*]pyridazines (1). A mixture of 1,4,5,7-tetramethyl-6-R^1-pyrrolo[3,4-*d*]pyridazine **2** (5 mmol), α-bromo ketone R_2COCH_2Br (5 mmol), and acetone (10 ml) was heated at reflux for 30 min. Then, water (10 ml) was added and $NaHCO_3$ (1.7 g, 20 mmol) was added in small portions while continuing heating. The reaction mixture was heated for a further 5 min. The precipitate formed was filtered off and recrystallized from *i*-BuOH–DMF. Yields 70-90%.

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1,2,3,4-Tetramethyl-8-phenyldipyrrolo[1,2-*b*:3,4-*d*]pyridazine (1a), mp 228-230°C (dec.). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm, (*J*, Hz): 2.51 (6H, s, 2Me); 2.56 (3H, s, N=CMe); 3.50 (3H, s, NMe); 6.55 (1H, d, *J* = 1.8, 9-CH); 7.16 (1H, t, *p*-H_{Ph}); 7.34 (2H, t, *m*-H_{Ph}); 7.58 (1H, d, *J* = 1.8, 7-CH); 7.62 (2H, d, *o*-H_{Ph}). Found, %: C 78.70; H 6.38; N 14.21. $C_{19}H_{19}N_3$. Calculated, %: C 78.86; H 6.62; N 14.52.

1,3,4-Trimethyl-8-phenyl-2-(4-tolyl)dipyrrolo[1,2-*b*:3,4-*d*]pyridazine (1b), mp 242-244°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm, (*J*, Hz): 2.31 (3H, s, Me); 2.34 (3H, s, Me); 2.46 (3H, s, Me_{Tol}); 2.61 (3H, s, N=CMe); 6.60 (1H, d, *J* = 1.7, 9-CH); 7.08-7.38 (7H, m, arom); 7.62-7.66 (3H, m, *o*-H_{Ph}, 7-CH). Found, %: C 81.89; H 6.07; N 11.33. $C_{25}H_{23}N_3$. Calculated, %: C 82.16; H 6.34; N 11.50.

7,9-Diacetyl-1,3,4-trimethyl-8-phenyl-2-(4-tolyl)dipyrrolo[1,2-*b*:3,4-*d*]pyridazine (3). Five drops of 70% aq. $HClO_4$ was added to a suspension of **1b** (0.37 g, 1 mmol) in acetic anhydride (5 ml). The mixture was heated slightly until the solid entered solution and then left at room temperature for 1.5 h. Then, water (10 ml) was added and the mixture was neutralized by adding $NaHCO_3$. The product was filtered off and crystallized from methanol–DMF to give 0.2 g (45%) of compound **3**; mp 206-208°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.94 (3H, s, COMe); 1.98 (3H, s, COMe); 2.40 (3H, s, Me); 2.45 (3H, s, Me); 2.47 (3H, s, Me_{Tol}); 2.69 (3H, s, N=CMe); 7.09 (2H, d, arom); 7.30-7.41 (7H, m, arom). IR spectrum (vaseline), ν, cm^{-1}: 1665 (C=O), 1630 (C=O). Found, %: C 77.23; H 5.86; N 9.07. $C_{29}H_{27}N_3O_2$. Calculated, %: C 77.48; H 6.05; N 9.35.

7,9-Diformyl-1,2,3,4-tetramethyl-8-phenyldipyrrolo[1,2-*b*:3,4-*d*]pyridazine (4). A mixture of **1a** (0.29 g, 1 mmol) and DMF (3 ml) was cooled on an ice bath and then, $POCl_3$ (0.37 ml, 4 mol) was added dropwise. The mixture was heated on a steam bath for 1 h. Then, water (20 ml) was added, followed by NaOAc (0.82 g). The mixture was heated at reflux for 10 min. After cooling, the precipitate was filtered off and crystallized from methanol–DMF to give 0.24 g (71%) of compound **4**; mp 250-252°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.60 (3H, s, Me); 2.71 (3H, s Me); 2.76 (3H, s, N=CMe); 3.71 (3H, s, NMe); 7.39-7.58 (5H, m, Ph); 9.76 (1H, s, 9-CHO); 10.07 (1H, s, 7-CHO). IR spectrum (vaseline), ν, cm^{-1}: 1660 (C=O). Found, %: C 72.81; H 5.28; N 11.98. $C_{21}H_{19}N_3O_2$. Calculated, %: C 73.03; H 5.54; N 12.17.

7-(4-Methoxyphenylazo)-1,3,4-trimethyl-8-phenyl-2-(4-tolyl)dipyrrolo[1,2-*b*:3,4-*d*]pyridazine (5). 4-Methoxyphenyldiazonium tetrafluoroborate (0.22 g, 1 mmol) was added to a solution of **1b** (0.37 g, 1 mmol) in DMF (5 ml) and heated for 5 min on a steam bath. Then, $NaHCO_3$ (0.17 g, 2 mmol) was added and the mixture was heated for an additional 5 min on a steam bath. After cooling, water (15 ml) was added. The precipitate was filtered off and crystallized from DMF to give 0.39 g (79%) of compound **5**; mp >220°C (dec.). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm, (*J*, Hz): 2.37 (3H, s, Me); 2.39 (3H, s, Me); 2.46 (3H, s, Me_{Tol}); 2.75 (3H, s, N=CMe); 3.84 (3H, s, OMe); 6.69 (1H, s, 9-CH); 6.94 (2H, d, *J* = 9.0, arom); 7.13 (2H, d, *J* = 8.2, arom); 7.25-7.47 (5H, m, Ph); 7.77-7.86 (4H, m, arom). Found, %: C 76.61; H 5.68; N 13.79. $C_{32}H_{29}N_5O$. Calculated, %: C 76.93; H 5.85; N 14.02.

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