1,3-Dipolar Cycloadditions of 2-Diazobutane, Diazophenylmethane and 1-Diazo-1-Phenylethane to Azolopyridazines. The Isolation of some Primary and Rearranged Cycloadducts and their Transformations into Substituted Pyrazolo[4,3-*d*]azolopyridazines

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The 1,3-dipolar cycloaddition of 2-diazobutane (**2**) to azolopyridazines **1** gave 9-ethyl-9-methyl-7,8-dihydropyrazolo[4,3-*d*]- **4** and 9-ethyl-9-methyl-9*H*-pyrazolo[4,3-*d*]azolopyridazines **5**. With diazophenylmethane (**6**) 7-benzyl-8-phenyl-7*H*- **12** and 8-benzyl-9-phenyl-8*H*-pyrazolo[4,3-*d*]azolopyridazines **13** were obtained, while with 1-diazo-1-phenylethane (**14**) the primary cycloadducts **15**, and rearranged cycloadducts **16** and **17** were isolated in some instances and further transformed into 9-methyl-9-phenyl-9*H*-pyrazolo[4,3-*d*]azolopyridazines **18**.

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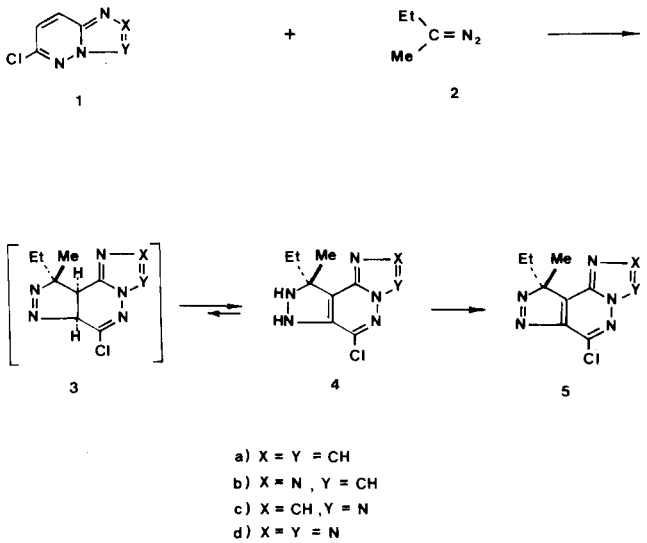
Recently, 1,3-dipolar cycloadditions of diazomethane and 2-diazopropane to imidazo[1,2-*b*]pyridazines [1-9], *s*-triazolo[4,3-*b*]pyridazines, *s*-triazolo[1,5-*b*]pyridazines, tetrazolo[1,5-*b*]pyridazines [2-8] and some other systems [11-13] have been extensively studied in our laboratory. The cycloadditions have been shown to be highly regiospecific to give in most cases only one, *i.e.* pyrazolo[4,3-*b*] fused azolo- and azinopyridazines, of the two possible isomers. Primary cycloadducts have not been isolated, since they are easily dehydrogenated in the presence of air. However, with diazomethane further methylation at either of the two nitrogen atoms of the newly formed pyrazole ring takes place to give two isomeric methyl derivatives [6].

In this communication we report the reactions of 6-chloroimidazo[1,2-*b*]- (**1a**), 6-chloro-*s*-triazolo[4,3-*b*]- (**1b**), 6-chloro-*s*-triazolo[1,5-*b*]- (**1c**), and 6-chlorotetrazolo[1,5-*b*]-pyridazine (**1d**) with 2-diazobutane (**2**), phenyldiazomethane (**6**) and 1-diazo-1-phenylethane (**14**). Since these diazoalkanes are less reactive than diazomethane or 2-diazopropane, we were able to isolate in some instances the primary CH,CH-dihydro cycloadducts and rearranged CH,NH- and NH,NH-dihydro intermediates. In the reaction of **1a-d** with **2** in diethyl ether at room temperature the primary 6a,9a-dihydro cycloadducts **3a-d** were not isolated, since they rearrange into 7,8-dihydro isomers **4a-d**, followed by oxidation in the presence of air, forming crude mixtures consisting of the corresponding pairs of **4a-d** and **5a-d**. The compounds **4a** and **4b** were not possible to separate from the mixture since they oxidize during the chromatographic procedure into **5a** and **5b**. On the other hand, **4c** and **4d** were isolated in pure forms and then oxidized with bromine in methanol or by heating in acetic acid under reflux to give **5c** and **5d**, respectively (Scheme 1).

Diazophenylmethane (**6**) is less reactive and therefore the reactions were carried out in more polar solvents and with large excess of the reagent. This consequently led to

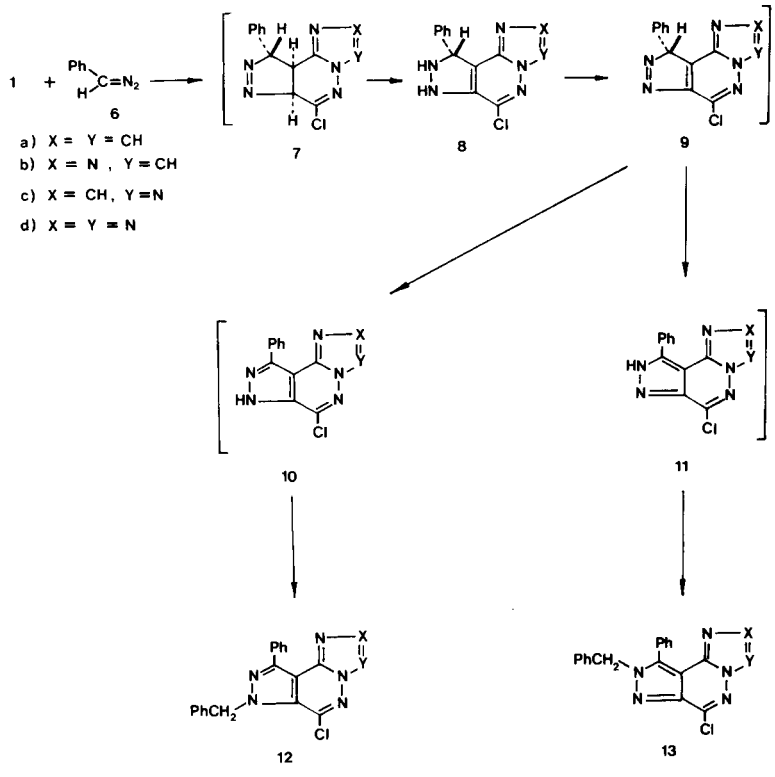
Scheme 1



further alkylation (benzylation) of the pyrazole part of the fused system. The compound **1a** does not react with phenyldiazomethane (**6**). The compounds **1b-d** react with **6** to give the mixtures of isomeric pairs of products **12b-d** and **13b-d**, benzylated at N_7 or N_8, respectively. The formation of these products can be explained by formation of the intermediates **10b-d** and their tautomeric forms **11b-d**, followed by further benzylation with an excess of **6** to give **12b-d** and **13b-d**, respectively (Scheme 2).

The structural assignments of these products are based on comparison of the ^{1}H nmr spectra (Table 1). The phenyl group at position 9 of **12b-d** shows two multiplets integrating for three and two protons, respectively. This indicates that 9-phenyl group is coplanar with the heterocyclic system and therefore we assume that the benzyl group is attached at position 7. On the other hand, in compounds **13b-d** the 9-phenyl group shows only a narrow multiplet, integrating for five protons, indicating that this group is

Scheme 2



no longer coplanar with the heterocyclic system, while the methylene protons of the benzyl group are shifted upfield, indicating thus that the benzyl group must be attached at position 8.

Table 1

^{1}H-NMR Data for Ph and CH_2Ph Groups in **12b-d** and **13a-d**

Compound	δ [ppm] 9-Ph	CH_2Ph	CH_2Ph
12b	7.37-7.65 (m, 3H) and 8.50-8.82 (m, 2H)	7.25 (br s, 5H)	6.05 (s, 2H)
12c	7.32-7.45 (m, 3H) and 8.40-8.60 (m, 2H)	7.19 (br s, 5H)	6.02 (s, 2H)
12d	7.37-7.67 (m, 3H) and 8.30-8.65 (m, 2H)	7.26 (br s, 5H)	6.10 (s, 2H)
13b	6.80-7.37 (m, 5H)	7.40-7.80 (m, 5H)	5.69 (s, 2H)
13c	6.92-7.41 (m, 5H)	7.41-7.87 (m, 5H)	5.76 (s, 2H)
13d	6.85-7.35 (m, 5H)	7.56 (br s, 5H)	5.76 (s, 2H)

The cycloaddition products with 1-diazo-1-phenylethane (**14**) are dependent on the structure of azolopyridazines. The compounds **1a** and **1c** react with **14** only when heated under reflux for several hours in a mixture of ethanol and petroleum ether, producing mixtures of **17a** and **18a**, and **17c** and **18c**, respectively, which can be separated by column chromatography to give pure components. On the other hand, cycloaddition of **14** to **1b** and **1d** took place at room temperature and primary 6a,9a-dihydro cycload-

Scheme 3

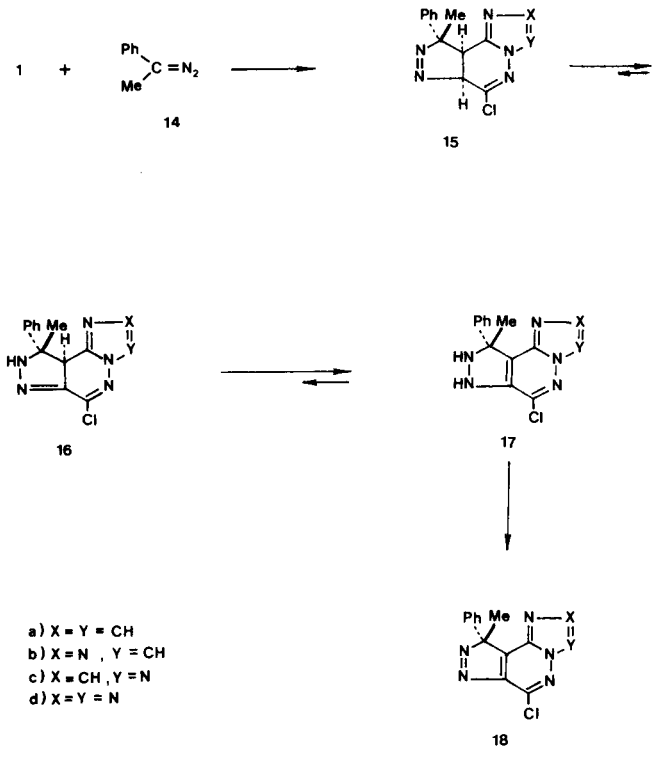


Table 2

^{1}H NMR Chemical Shifts for 6a-H, 8-H, and 9a-H and **15b,d** and **16b,d**

Compound	Solvent	δ [ppm] 6a-H	8-H	9a-H	J
15b	$CDCl_3$	4.53 (d)	–	5.76 (d)	6.0 Hz
15d	$CDCl_3$	4.39 (d)	–	5.94 (d)	6.0 Hz
16b	DMSO-d_6	–	8.15 (br s)	5.73 (s)	–
16d	DMSO-d_6	–	9.02 (br s)	6.0 (s)	–

ducts **15b** and **15d** were isolated in pure forms. However, these two compounds are stable in these forms only in non-polar solvents and they can be observed in ^{1}H nmr spectra in deuteriochloroform solution, while in DMSO-d_6 they rearrange into 8,9a-dihydro tautomeric forms **16b** and **16d**, respectively (Table 2) (Scheme 3).

The structures of compounds mentioned here were also confirmed by some thermal and photochemical transformations. The results will be published separately.

EXPERIMENTAL

Melting points were taken on a Kofler micro stage. All ^{1}H nmr spectra were obtained on a JEOL JNM C-60-HL spectrometer, and micro analyses for C, H, and N on a Perkin-Elmer Analyser 240 C.

The following compounds were prepared according to the procedures described in the literature: 6-chloroimidazo[1,2-*b*]pyridazine (**1a**) [14] 6-chloro-*s*-triazolo[4,3-*b*]pyridazine (**1b**) [15], 6-chloro-*s*-triazolo[1,5-*b*]pyridazine (**1c**) [16], 6-chlorotetrazolo-[1,5-*b*]pyridazine (**1d**) [15], 2-diazobutane (**2**) [17], diazophenylmethane (**6**) [20], and 1-diazo-1-phenylethane (**14**) [21]. The reactions were followed by tlc (DC Fertigplatten Kieselgel 60 F-254, E. Merck. Darmstadt, and a mixture of chloroform and methanol, 10:1, as solvent).

6-Chloro-9-ethyl-9-methyl-7,8-dihydro-9*H*-imidazo[1,2-*b*]pyrazolo-[4,3-*d*]pyridazine (**4a**) and 6-Chloro-9-ethyl-9-methyl-9*H*-imidazo-[1,2-*b*]pyrazolo[4,3-*d*]pyridazine (**5a**).

To a solution of 2-diazobutane (~5 g) in diethyl ether (70 ml) **1a** (500 mg) was added and the mixture was stirred for three days at room temperature. The reaction was followed by tlc, until all the starting material was consumed. The volatile components were evaporated *in vacuo*. Ethanol (10 ml) was added to the residue and the solution was evaporated to dryness. This was repeated several times, until crystalline material was obtained. The ^{1}H nmr spectrum shows that the crude product is a mixture of **4a** and **5a**. The transformation of **4a** into **5a** was carried out in the following way. The crude product was suspended in methanol (10 ml) and solution of bromine (1 g) in methanol (10 ml) was added dropwise until **4a** was completely transformed into **5a**. The reaction mixture was refrigerated and the precipitate was collected by filtration to give **5a** (600 mg, 79%), mp 113-114° (from DMSO); ^{1}H nmr (deuteriochloroform): **4a** δ 0.96 (t, *Me*CH_2), 1.71 (s, Me), 1.03 (q) and 2.08 (q) (Me*C*H_2), 4.2 (br s, NH), 5.6 (br s, NH), 7.64 (d, H_2), 7.86 (d, H_3), J_{MeCH_2} = 7.3 Hz, J_{H_2,H_3} = 1.4 Hz; ^{1}H nmr (deuteriochloroform): **5a** δ 0.62 (t, *Me*CH_2), 1.80 (s, Me), 2.45 (q) and 2.55 (q) (Me*C*H_2), 7.89 (d, H_2), 8.07 (d, H_3), J_{MeCH_2} = 7.3 Hz, J_{H_2,H_3} = 1.3 Hz.

Anal. Calcd. for $C_{10}H_{10}ClN_5$: C, 50.96; H, 4.28; N, 29.72. Found: C, 51.19; H, 4.29; N, 29.75.

6-Chloro-9-ethyl-9-methyl-9*H*-pyrazolo[4,3-*d*]-*s*-triazolo[4,3-*b*]-pyridazine (**5b**).

To a solution of **2** (~5 g) in ether (70 ml) **1b** (1.54 g) was added and the mixture was stirred for one hour at room temperature. The solution was evaporated to one third *in vacuo* and the yellow precipitate was collected by filtration to give (2.05 g) of the crude product. This material (239 mg) was dissolved in ethanol (5 ml) and a solution of bromine (10% in ethanol) was added dropwise until the color of bromine persisted. Aqueous solution of ammonia (10%, 2 ml) was added and the mixture was left in refrigerator overnight. The precipitate was collected by filtration to give **5b** (169 mg, 71%), mp 179-180° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 0.69 (t, 9-CH_2*Me*), 1.84 (s, 9-Me), 2.51 (q, 9-C*H*$_2$Me), 9.18 (s, H_3), J_{CH_2Me} = 7.0 Hz.

Anal. Calcd. for $C_9H_9ClH_6$: C, 45.68; H, 3.83; N, 35.51. Found: C, 46.02; H, 4.01; N, 35.70.

6-Chloro-9-ethyl-9-methyl-7,8-dihydro-9*H*-pyrazolo[4,3-*d*]-*s*-triazolo[1,5-*b*]pyridazine (**4c**).

To a suspension of **1c** (1.0 g) in ether (20 ml) a solution of **2**, prepared from 2-butanone hydrazone (6 g) in ether (70 ml), was added and the mixture was stirred at room temperature for two hours. The solution was evaporated to one-third and the precipitate was collected by filtration to give **4c** (910 mg, 59%), mp 140-141° (from xylene); ^{1}H nmr (deuteriochloroform): δ 0.96 (t, 9-CH_2*Me*), 1.7 (s, 9-Me), 1.95 (q, 9-C*H*$_2$Me), 4.32 (br s, NH), 8.3 (s, H_2), J_{MeCH_2} = 7.2 Hz.

Anal. Calcd. for $C_9H_{11}ClN_6$: C, 45.29; H, 4.65; N, 35.21. Found: C, 45.26; H, 4.67; N, 35.34.

6-Chloro-9-ethyl-9-methyl-9*H*-pyrazolo[4,3-*d*]-*s*-triazolo[1,5-*b*]-pyridazine (**5c**).

Method A.

To a suspension of **1c** (300 mg) in ethanol (10 ml) a solution of **2**, prepared from 2-butanone hydrazone (7 g), in ether (30 ml), was added and the mixture was stirred at room temperature for two hours. The volatile components were evaporated *in vacuo*, ethanol (10 ml) was added to the oily residue, and the resulting solution left in refrigerator for 20 days. The precipitate was collected by filtration to give **5c** (165 mg, 36%), mp 123-125° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 0.67 (t, *Me*CH_2), 1.80 (s, Me), 2.45 (q) and 2.50 (q) (Me*C*H_2), 8.52 (s, H_2), J_{MeCH_2} = 7.2 Hz.

Anal. Calcd. for $C_9H_9ClN_6$: C, 45.68; H, 3.83; N, 35.50. Found: C, 45.66; H, 3.91; N, 35.25.

Method B.

To a solution of **4c** (400 mg) in methanol bromine (10% in methanol) was added dropwise during stirring until the color of bromine persisted. The precipitate was collected by filtration to give **5c** (325 mg, 82%). The compound was identical with the compound prepared according to method A.

Method C.

A suspension of **4c** (200 mg) in acetic acid (5 ml) was heated under reflux for 6 hours. The solvent was evaporated and the solid residue purified by column chromatography (Kieselgel 60, 0.040-0.063 mm, E. Merck, and diethyl ether as solvent). The sol-

vent was evaporated *in vacuo* to give **5c** (140 mg, 71%). The compound was identical with the compound prepared according to the method A.

6-Chloro-9-ethyl-9-methyl-7,8-dihydro-9*H*-pyrazolo[4,3-*d*]tetrazolo[1,5-*b*]pyridazine (**4d**).

To a solution of **2**, prepared from 2-butanone hydrazone (4 g) in ether (80 ml), **1d** (1 g) was added and the mixture was stirred for 40 minutes at room temperature. The yellow precipitate was collected by filtration to give **4d** (1.25 g, 81%), mp 134-135° (from xylene); ^{1}H nmr (deuteriochloroform): δ 0.98 (t, *Me*CH$_2$), 1.74 (s, Me), 2.97 (q) and 3.02 (q) (MeC*H*$_2$), 4.15-5.0 (br s, NH), 6.0-6.55 (br s, NH).

Anal. Calcd. for $C_8H_{10}ClN_7$: C, 40.09; H, 4.21; N, 40.91. Found: C, 40.32; H, 4.32; N, 41.20.

6-Chloro-9-ethyl-9-methyl-9*H*-pyrazolo[4,3-*d*]tetrazolo[1,5-*b*]pyridazine (**5d**).

To a suspension of **4d** (400 mg) in methanol (10 ml) a solution of bromine (10% in methanol) was added dropwise until the color of bromine persisted. The solution was neutralized with ammonia (28%). The volatile components were evaporated *in vacuo* and the solid residue was purified by column chromatography (Kieselgel 60, 0.040-0.063 mm, E. Merck and diethyl ether as solvent). Evaporation of ether *in vacuo* gave **5d** (315 mg, 79%), mp 96-98° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 0.75 (t, *Me*CH$_2$), 1.89 (s, Me), 2.52 (q, MeC*H*$_2$), J_{MeCH_2} = 7.5 Hz.

Anal. Calcd. for $C_8H_8ClN_7$: C, 40.43; H, 3.39; N, 41.26. Found: C, 40.61; H, 3.41; N, 41.65.

7-Benzyl-6-chloro-9-phenyl-7*H*-pyrazolo[4,3-*d*]-*s*-triazolo[4,3-*b*]pyridazine (**12b**) and 8-Benzyl-6-chloro-9-phenyl-8*H*-pyrazolo[4,5-*d*]-*s*-triazolo[4,3-*b*]pyridazine (**13b**).

To a solution of **1b** (1 g) in ethanol (30 ml) a solution of **6**, prepared from benzaldehyde hydrazone (15 g) in petroleum ether (80 ml), was added and the mixture was heated under reflux for 15 hours. The mixture was left in refrigerator for several days. The precipitate, formed during this time, was collected by filtration to give after recrystallization from ethanol **13b** (640 mg, 27%), mp 181-183°; ^{1}H nmr (DMSO-d$_6$): δ 5.69 (s, C*H*$_2$Ph), 6.80-7.37 (m, 9-Ph), 7.4-7.8 (m, CH$_2$*Ph*), 9.34 (s, H$_3$).

Anal. Calcd. for $C_{19}H_{13}ClN_6$: C, 63.25; H, 3.63; N, 23.29. Found: C, 63.10; H, 3.62; N, 23.33.

When the above reaction mixture was, after heating, evaporated *in vacuo*, the oily residue was obtained. Diethyl ether (50 ml) was added to this residue and the precipitate, which formed after several hours, was collected by filtration to give **12b** (110 mg, 16%), mp 165° (from ethanol); ^{1}H nmr (DMSO-d$_6$): 150° δ 6.05 (s, C*H*$_2$Ph), 7.28 (s, CH$_2$*Ph*), 7.37-7.65 (m) and 8.50-8.82 (m) (9-Ph), 9.40 (s, H$_3$).

Anal. Calcd. for $C_{19}H_{11}ClN_6$: C, 63.25; H, 3.63; N, 23.29. Found: C, 63.31; H, 3.72; N, 23.17.

7-Benzyl-6-chloro-9-phenyl-7*H*-pyrazolo[4,3-*d*]-*s*-triazolo[1,5-*b*]pyridazine (**12c**) and 8-Benzyl-6-chloro-9-phenyl-8*H*-pyrazolo[4,3-*d*]-*s*-triazolo[1,5-*b*]pyridazine (**13c**).

To a solution of **1c** (1.0 g) in ethanol (40 ml) a solution of **6**, prepared from benzaldehyde hydrazone (8 g) in petroleum ether, was added and the mixture was stirred at room temperature for 24 hours. An equal portion of **6** was added again and the mixture was heated, until all the starting material was consumed. The solvent was evaporated *in vacuo* and the oily residue was left at room temperature for three weeks. The solid was collected by filtration, washed with ethanol and recrystallized from DMF to give **12c** (385 mg, 16%), mp 218-220°; ^{1}H nmr (DMSO-d$_6$): δ 6.02 (br s, PhC*H*$_2$), 7.19 (br s, *Ph*CH$_2$), 7.32-7.45 (m) and 8.40-8.60 (m) (9-Ph), 8.39 (s, H$_2$).

Anal. Calcd. for $C_{19}H_{13}ClN_6$: C, 63.25; H, 3.63; N, 23.29. Found: C, 62.84; H, 3.69; N, 23.00.

The filtrate was evaporated to one-third, the precipitate, formed in refrigerator after several hours, was collected by filtration and purified by column chromatography (silica gel and a mixture of ether and petroleum ether, 1:2) to give **13c** (250 mg, 22%), mp 184-185°; ^{1}H nmr (DMSO-d$_6$): δ 5.78 (s, PhC*H*$_2$), 6.92-7.41 (m, 9-Ph), 7.41-7.87 (m, *Ph*CH$_2$), 8.34 (s, H$_2$).

Anal. Calcd. for $C_{19}H_{13}ClN_6$: C, 63.25; H, 3.63; N, 23.29. Found: C, 63.62; H, 3.70; N, 23.42.

7-Benzyl-6-chloro-9-phenyl-7*H*-pyrazolo[4,3-*d*]tetrazolo[1,5-*b*]pyridazine (**12d**).

To a solution of **1d** (300 mg) in ethanol (10 ml) a solution of **6**, prepared from benzaldehyde hydrazone (4 g) in petroleum ether (35 ml), was added and the mixture was stirred at room temperature for 20 hours. The solvents were evaporated *in vacuo*. The precipitate, formed after addition of diethyl ether (20 ml) to the oily residue, was collected by filtration to give **12d** (265 mg, 38%), mp 239-241° (from DMF); ^{1}H nmr (DMSO-d$_6$): 145° δ 6.10 (s, C*H*$_2$Ph), 7.26 (s, CH$_2$*Ph*), 7.37-7.67 (m) and 8.30-8.65 (m) (9-Ph).

Anal. Calcd. for $C_{18}H_{12}ClN_7$: C, 59.76; H, 3.34; N, 27.10. Found: C, 59.67; H, 3.42; N, 27.01.

8-Benzyl-6-chloro-9-phenyl-8*H*-pyrazolo[4,3-*d*]tetrazolo[1,5-*b*]pyridazine (**13d**).

To a solution of **1d** (1 g) in ethanol (20 ml) a solution of **6**, prepared from benzaldehyde hydrazone (20 g) in petroleum ether (30 ml), was added and the mixture was stirred at room temperature for 12 hours. The precipitate formed during this time was collected by filtration to give **12d** (420 mg, 18%). The filtrate was heated under reflux for 5 hours, until all starting material reacted. The solvents were evaporated *in vacuo* and the residue was purified by column chromatography (Kieselgel 60, 0.040-0.063, E. Merck, and a mixture of diethyl ether and petroleum ether, 1:3, as solvent) to give, after evaporation of the solvents *in vacuo*, **13d** (330 mg, 14%), mp 151-153° (from cyclohexane); ^{1}H nmr (DMSO-d$_6$): δ 5.76 (s, C*H*$_2$Ph), 6.85-7.35 (m, 9-Ph), 7.56 (br s, CH$_2$*Ph*).

Anal. Calcd. for $C_{18}H_{12}ClN_7$: C, 59.76; H, 3.34; N, 27.10. Found: C, 59.73; H, 3.48; N, 27.19.

6-Chloro-9-methyl-9-phenyl-7,8-dihydro-9*H*-imidazo[1,2-*b*]pyrazolo[4,3-*d*]pyridazine (**17a**) and 6-Chloro-9-methyl-9-phenyl-9*H*-imidazo[1,2-*b*]pyrazolo[4,3-*d*]pyridazine (**18a**).

To a solution of **1a** (1 g) in ethanol (50 ml) a solution of **14**, prepared from acetophenone hydrazone (8 g), in petroleum ether (100 ml), was added. The mixture was heated under reflux for 10 hours. An equal portion of **14** was added, and the heating was continued for 30 hours. The precipitate, identified as acetophenone azine, was, after cooling, filtered off and discarded, the filtrate was evaporated *in vacuo* and the dry residue separated into two components by column chromatography (Kieselgel 60, 0.040-0.063 mm, E. Merck, and a mixture of diethyl ether and petroleum ether, 3:1, as eluent). The first fraction gave, after

evaporation of the solvent, **17a** (403 mg, 22%), mp 141-144° (hexane); ^{1}H nmr (deuteriochloroform): δ 2.07 (s, 9-Me), 7.05-7.37 (m, H_3, $H_{4'}$, $H_{5'}$), 7.62-7.87 (m, $H_{2'}$, $H_{6'}$), 7.62 (d, H_2), 7.80 (d, H_3), J_{H_2,H_3} = 1.5 Hz.

Anal. Calcd. for $C_{14}H_{12}ClN_5$: C, 58.85; H, 4.23; N, 24.51. Found: C, 58.72; H, 4.40; N, 24.32.

The second fraction gave, after evaporation of the solvent, **18a** (424 mg, 23%), mp 98-100° (hexane); ^{1}H nmr (deuteriochloroform): δ 2.10 (s, 9-Me), 7.25-7.48 (m, $H_{3'}$, $H_{4'}$, $H_{5'}$), 7.62-7.85 (m, $H_{2'}$, $H_{6'}$), 7.98 (d, H_2), 8.12 (d, H_3), J_{H_2,H_3} = 1.5 Hz.

Anal. Calcd. for $C_{14}H_{10}ClN_5$: C, 59.27; H, 3.55; N, 24.68. Found: C, 59.09; H, 3.65; N, 24.57.

6-Chloro-9-methyl-9-phenyl-6a,9a-dihydro-9*H*-pyrazolo[4,3-*d*]-*s*-triazolo[4,3-*b*]pyridazine (**15b**).

To a suspension of **1b** (1.0 g) in petroleum ether (10 ml) a solution of **14**, prepared from acetophenone hydrazone (8 g) in petroleum ether (30 ml), was added and the mixture was stirred for 3 hours at room temperature. The solvent was evaporated *in vacuo* to one-half, and the product was collected by filtration to give **15b** (1.45 g, 78%), mp 166-167° (from benzene); ^{1}H nmr (deuteriochloroform): δ 2.12 (s, 9-Me), 4.53 (d, H_{6a}), 5.76 (d, H_{9a}), 7.15-7.40 (m) and 7.70-7.80 (m) (Ph), 8.95 (s, H_3), $J_{H_{6a},H_{9a}}$ = 6.0 Hz; ^{1}H nmr (DMSO-d_6): (tautomeric form **16b**) δ 2.06 (s, 9-Me), 5.73 (br s, 9a-H), 7.12-7.42 (m) and 7.65-7.78 (m) (9-Ph), 8.15 (br s, NH), 8.93 (s, H_3).

Anal. Calcd. for $C_{13}H_{11}ClN_6$: C, 54.46; H, 3.87; N, 29.31. Found: C, 54.08; H, 3.86; N, 28.94.

6-Chloro-9-methyl-9-phenyl-7,8-dihydro-9*H*-pyrazolo[4,3-*d*]-*s*-triazolo[1,5-*b*]pyridazine (**17c**) and 6-Chloro-9-methyl-9-phenyl-9*H*-pyrazol0[4,3-*d*]-*s*-triazolo[1,5-*b*]pyridazine (**18c**).

To a solution of **1c** (2.0 g) in a mixture of chloroform and diethyl ether (1:1, 30 ml) a solution of **14**, prepared from acetophenone hydrazone (8 g) in petroleum ether (50 ml), was added and the mixture was stirred for 12 hours at room temperature followed by heating under reflux for one hour. The solvents were removed by evaporation *in vacuo*, ethanol (25 ml) was added to the oily residue and the solid acetophenone azine was filtered off. The filtrate was evaporated *in vacuo* and the dry residue was separated by column chromatography (Kieselgel 60, 0.040-0.063 mm, E. Merck, and the mixture of diethyl ether and petroleum ether, 3:1, for elution of the first fraction, and 1:3 for elution of the second fraction). The first fraction gave, after evaporation of solvents **18c** (0.7 g, 19%), mp 125-126° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 2.11 (s, 9-Me), 7.07-7.43 (m, $H_{3'}$, $H_{4'}$, $H_{5'}$), 7.45-7.85 (m, $H_{2'}$, $H_{6'}$), 8.58 (s, H_2).

Anal. Calcd. for $C_{13}H_9ClN_6$: 54.84; H, 3.19; N, 29.52. Found: C, 54.64; H, 3.32; N, 29.27.

The second fraction gave, after evaporation of the solvents, **17c** (1.4 g, 38%), mp 150-152° (from a mixture of ethanol and hexane); ^{1}H nmr (deuteriochloroform): δ 2.06 (s, 9-Me), 3.9-5.0 (br s, NH), 6.85-7.35 (m, $H_{3'}$, $H_{4'}$, $H_{5'}$), 7.45-7.80 (m, $H_{2'}$, $H_{6'}$).

Anal. Calcd. for $C_{13}H_{11}ClN_6$: C, 54.46; H, 3.87; N, 29.31. Found: C, 54.52; H, 4.03; N, 29.06.

Oxidation of **17c** into **18c** in Acetic Acid.

To a solution of **17c** (500 mg) in acetic acid (15 ml) a solution of bromine in acetic acid (10%) was added dropwise until the color of bromine persisted. The solvent was evaporated *in vacuo*, washed with water and recrystallized from ethanol to give **18c** (420 mg, 85%). The compound was identical in all respects with the compound obtained above.

6-Chloro-9-methyl-9-phenyl-6a,9a-dihydro-9*H*-pyrazolo[4,3-*d*]-tetrazolo[1,5-*b*]pyridazine (**15d**).

To a solution of **1c** (6.0 g) in diethyl ether (30 ml) a solution of 1-diazo-1-phenylethane, prepared from acetone hydrazone (50 g) in petroleum ether (200 ml) was added and it was stirred for four hours at room temperature. The precipitate was collected by filtration and washed with diethyl ether to give **15d** (10.5 g, 95%), mp 165-166° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 2.13 (s, 9-Me), 4.39 (d, H_{6a}), 5.94 (d, H_{9a}), 7.16-7.40 (m, $H_{3'}$, $H_{4'}$, $H_{5'}$), 7.62-7.87 (m, $H_{2'}$, $H_{6'}$); ^{1}H nmr (DMSO-d_6): (tautomeric form **16d**) δ 2.0 (s, 9-Me), 6.0 (m, 9a-H), 7.15-7.47 (m) and 7.60-7.85 (m) (9-Ph), 9.02 (br s, NH).

Anal. Calcd. for $C_{12}H_{10}ClN_7$: C, 50.10; H, 3.50; N, 34.09. Found: C, 50.38; H, 3.47; N, 34.05.

6-Chloro-9-methyl-9-phenyl-9*H*-pyrazolo[4,3-*d*]-*s*-triazolo[4,3-*b*]-pyridazine (**18b**).

Method A.

To a solution of **1b** (1.0 g) in ethanol, a solution of **14**, prepared from acetophenone hydrazone (8 g) in petroleum ether (30 ml), was added and the mixture was stirred for 20 hours at 40°. The solvent was evaporated *in vacuo*, ethanol (30 ml) was added to the oily residue and the solid acetophenone azine was filtered off. The filtrate was evaporated *in vacuo* and the crude product was purified by column chromatography (Kieselgel 60, 0.040-0.063 mm, E. Merck, and a mixture of diethyl ether and petroleum ether, 3:1, as eluent), to give, after evaporation of the solvents, **18b** (1.25 g, 68%), mp 64-69° (from hexane); ^{1}H nmr (deuteriochloroform): δ 2.14 (s, 9-Me), 7.21-7.47 (m, $H_{3'}$, $H_{4'}$, $H_{5'}$), 7.52-7.90 (m, $H_{2'}$, $H_{6'}$), 9.19 (s, H_3).

Anal. Calcd. for $C_{13}H_9ClN_6$: C, 54.84; H, 3.19; N, 29.52. Found: C, 54.82; H, 3.25; N, 29.44.

Oxidation of **17b** with Air.

Method B.

A solution of **17b** (200 mg) in ethanol (5 ml) was left in an open flask for 10 days at room temperature. Ethanol was evaporated *in vacuo* and the oily residue was purified by column chromatography as above, to give **18b** (126 mg, 63%). The compound was identical in all respects with the compound prepared according to Method A.

6-Chloro-9-methyl-9-phenyl-9*H*-pyrazolo[4,3-*d*]tetrazolo[1,5-*b*]-pyridazine (**18d**).

Method A.

To a solution of **1d** (300 mg) in DMF (10 ml) a solution of **14**, prepared from acetophenone hydrazone (3 g), in petroleum ether (6 ml), was added and the mixture was stirred for two days at room temperature. The solvents were evaporated *in vacuo*, ethanol (5 ml) was added to the residue and the solid acetophenone azine was filtered off. The filtrate was evaporated *in vacuo* and purified by column chromatography (Kieselgel, 60, 0.040-0.063 mm, E. Merck, and a mixture of diethyl ether and petroleum ether, 3:1, as eluent) to give, after evaporation of the solvents **18d** (265 mg, 48%), mp 149-150° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 2.18 (s, 9-Me), 7.25-7.50 (m, $H_{3'}$, $H_{4'}$, $H_{5'}$), 7.54-7.82

(m, $H_{2''}$, $H_{6'}$).

Anal. Calcd. for $C_{12}H_8ClN_7$: C, 50.45; H, 2.82; N, 34.32. Found: C, 50.12; H, 2.80; N, 34.20.

Oxidation with Bromine.

Method B.

To a solution of **15d** (2.88 g) in acetic acid (20 ml) a solution of bromine in acetic acid (10%) was added dropwise until the color of bromine persisted. The solvent was evaporated *in vacuo* and the solid residue recrystallized from ethanol to give **18d** (260 g, 91%). The compound was identical in all respects with the compound prepared above.

Oxidation with Hydrogen Peroxide.

Method C.

To a solution of **15d** (288 mg) in ethanol (10 ml) a solution of hydrogen peroxide (aqueous solution, 30%, 0.5 ml) was added and the mixture was left at room temperature for several hours. The precipitate, formed during this time, was collected by filtration and recrystallized from ethanol to give **18d** (98 mg, 34%). The compound was identical with that described above.

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