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Dehydration of 2-(2-Arylethyl)-2-hydroxy-4-oxopentanoic Acids and Their Hydrazones to Form Heterocycles [1]

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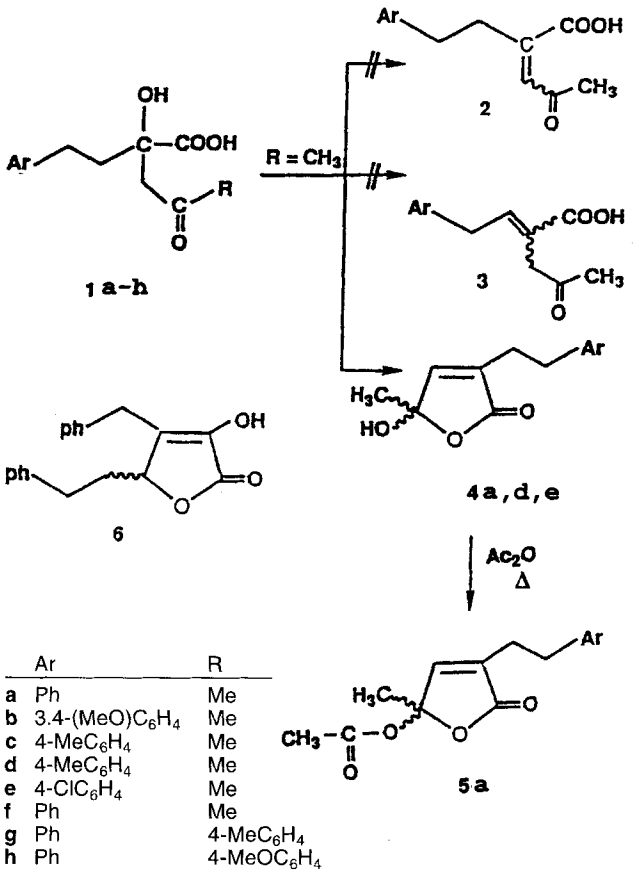
Dedicated to Prof. Dr. Hans Zimmer on the Occasion of his 75th Birthday

Abstract. Dehydration of 2-(2-arylethyl)-2-hydroxy-4-oxopentanoic acids **1** with hydrochloric acid/acetic acid, affords 3-(2-arylethyl)-5-hydroxy-5-methyl-2(5*H*)-furanones **4**. Compounds of type **1** and **4** represent suitable precursors for the formation of pyridazin-3-ones **7** as they smoothly react with hydrazine. A new series of *s*-triazolo[4,3-*b*]pyridazin-3-ones **12** and tetrazolo[1,5-*b*]pyridazines **15** are obtained from the 3-chloropyridazines **11** upon treatment with semicarbazide and sodium azide, respectively. Reaction of **11** with phenyl- acetylhydrazine provides 3-benzyl-6-phenyl-8-(2-phenyl- ethyl)-*s*-triazolo[4,3-*b*]pyridazine **13** *via* dehydrative cyclization of the intermediate **14** which was clarified to exhibit tautomeric equilibria between enol–hydrazine form **A** and keto–hydrazine form **B** by means of ^{1}H and ^{13}C NMR spectroscopy. Attempts to synthesize 3-alloxy-pyridazines **18** by reacting **11** with sodium alloxide afford *N*-allyl compounds **17**.

Within a project dealing with the synthesis of substituted pyridazines, the 2-(2-arylethyl)-2-hydroxy-4-substituted butanoic acids **1** were approached as intermediates [2–4]. They were first reported by Bougault [5] from the reaction of functionalized pyruvic acids with methyl aryl(methyl) ketones in aqueous ethanolic alkaline medium. This author also investigated the dehydration of **1a** with hydrochloric acid and claimed to obtain an acid, $C_{13}H_{14}O_3$ of *m.p.* 95 °C of unknown structure. Later Cordier and Hathout [6] obtained a mixture of ethylenic acids **2b** and **3b** when **1b** was heated with dilute hydrochloric acid at 100 oc for one hour. In 1967, Cordier [7] reported that **1c** was readily dehydrated in a hydrochloric acid/acetic acid mixture to yield the corresponding 4-oxopent-2-enoic acid **2c** which could be isomerized to **3c** upon using higher acid concentration or longer acid treatment. These findings as well as the high possibility of **1** to undergo 5-*exo*-trig-cyclization to give pseudo acids of structure **4** [8, 9] prompted us to reinvestigate the dehydration of **1a** using a hydrochloric acid/acetic acid mixture. In our hands, a single colourless product of *m.p.* 92–93 °C was formed. Although its elemental analysis is in agreement with the elimination of one molecule of water from its precursor, its structure is not in agreement with those reported earlier for its analogs as **2a** or **3a**. Its structural assignment as **4a** is deduced from the following evidence: ^{1}H NMR showed the methyl protons (δ= 1.60 ppm) as a singlet, the ethano-fragment protons (δ = 2.57 and 2.86 ppm) as multiplet and triplet, the alcoholic proton (δ=4.32 ppm) as a singlet which underwent deuterium oxide exchange, the C-4 proton (δ = 6.69 ppm) as a triplet which shows long-range coupling (^3J = 1.52 Hz); undecoupled and DEPT ^{13}C NMR revealed the presence of eleven unique carbons where four carbons are quaternary; fully proton-coupled ^{13}C NMR showed C-2 (δ =171.74 ppm) as a doublet of triplet (^3J= 13.3, 4.1 Hz); Finally, heating **4a** in acetic anhydride led to the formation of its *O*-acetyl derivative **5a** (Scheme 1).

Similarly, the dehydration of **1d** and **1e** led to the formation of their corresponding **4d** and **4e**.

Heating a solution of **4a** in 36% hydrochloric acid for four hours on a water bath afforded **6.** A plausible mechanism for the formation of **6** might involve the



	Ar	R
a	Ph	Me
b	3.4-(MeO)C_6H_4	Me
c	4-MeC_6H_4	Me
d	4-MeC_6H_4	Me
e	4-ClC_6H_4	Me
f	Ph	Me
g	Ph	4-MeC_6H_4
h	Ph	4-$MeOC_6H_4$

Scheme 1

regeneration of benzylpyruvic acid which underwent acid-catalyzed Aldol condensation, lactonization, followed by decarboxylation. In order to cross examine this assumption, benzylpyuric acid was heated with 36% hydrochloric acid, and the reaction was monitored by TLC which indeed showed the formation of **6**.

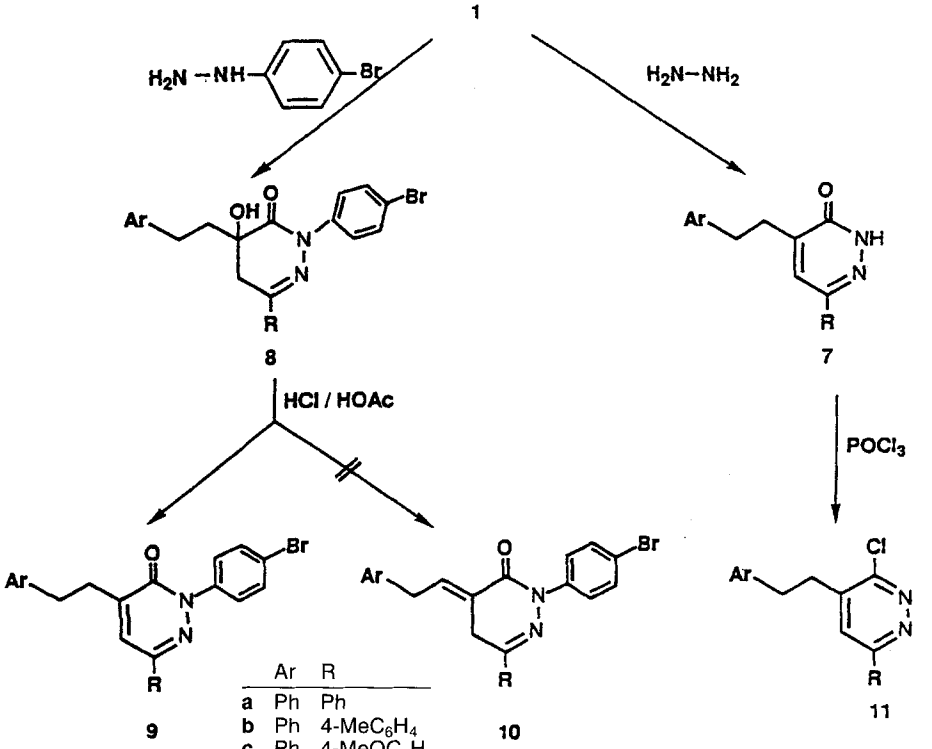
Treatment of compounds **1** or **4** with hydrazine hydrate and few drops of acetic acid in ethanol afforded the 2,3-dihydropyridazin-3-ones **7** (Scheme 2).

Reaction of **1** with *p*-bromophenylhydrazine afforded the 2,3,4,5-tetrahydropyridazin-3-ones **8**. Dehydration of **8** by heating in a mixture of hydrochloric acid and acetic acid gives **9.** The alternative structure **10**, containing the exocyclic double bond was ruled out on the basis of the spectral data (see experimental section).

The pyridazinones **7** were converted into the corresponding chloro compounds **11** in good yields on treatment with phosphoryl chloride.

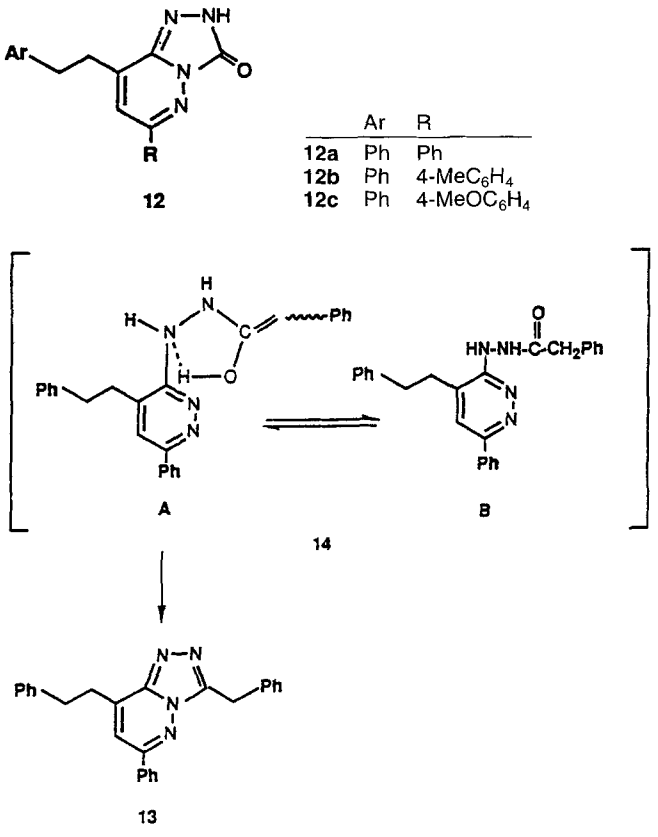
Treatment of **11** with semicarbazide hydrochloride and a few drops of hydrochloric acid gave the corresponding *s*-triazolo[4,3-*b*]pyridazin-3-ones **12** (Scheme 3).

Reaction of **11** with phenylacetylhydrazine led to the expected 3-benzyl-6-phenyl-8-(2-phenylethyl)-*s*-triazolo[4,3-*b*]pyridazine **13.** The structural assignment was based on spectroscopic data and elemental analysis (see experimental section). The reaction intermediate was isolated after short period of heating. It was identified as a mixture of enol-hydrazine and keto-hydrazine tautomer forms **14A** and **14B** as evidenced by its NMR



	Ar	R
a	Ph	Ph
b	Ph	4-MeC_6H_4
c	Ph	4-$MeOC_6H_4$
d	Ph	Me

Scheme 2



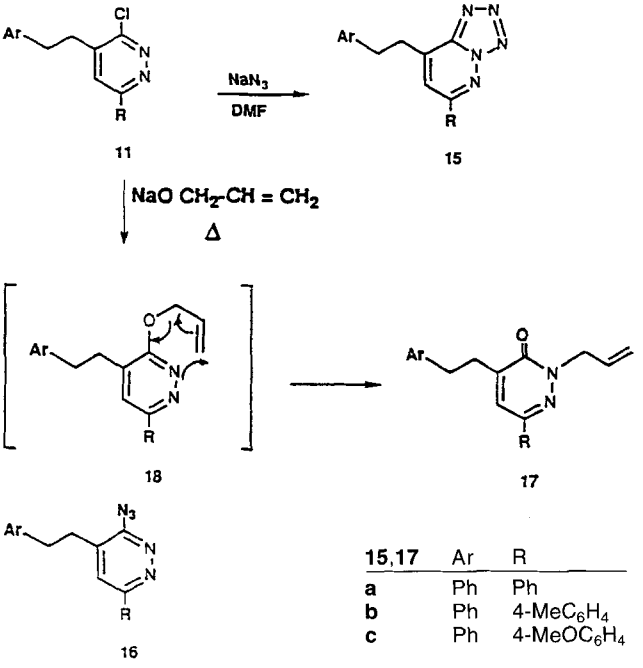
Scheme 3

spectra [10]. ^{1}H NMR ($CDCl_3$) showed the ethano-fragment as a multiplet and two unsymmetrical triplets (δ = 3.01 ppm, 3.72 and 3.43 ppm). The olefinic proton of form **A** appeared as a singlet at δ=7.11 ppm, while the methylene group protons of form **B** caused a singlet at δ=4.63. Structure determination of this intermediate was unambiguously established by means of ^{13}C NMR spectroscopy. The spectra exhibited five different CH_2 groups at 30.74, 31.87, 32.61, 33.49 and 43.13 ppm. The olefinic carbon of form **A** caused a band at δ = 116.84 ppm while the amide carbon of form **B** appeared at δ= 161.97 ppm.

Compounds **11** were converted into the corresponding tetrazolo[1,5-*b*]pyridazines **15** on reaction with sodium azide in *N*,*N*-dimethyl formamide. The structure of compounds **15** was supported by IR spectroscopy which showed the absence of an absorption band in the region 2160–2120 cm^{-1} characteristic for the presence of an azide group of the alternative structure **16**.

Treatment of **11** with sodium alloxide in allyl alcohol afforded a colourless product in each case. Their infrared spectra showed a band in the region of 1604–1615 cm^{-1} attributed to the frequency of C=N group and a band in the amide carbonyl frequency region at 1649–1652 cm^{-1}. These data indicated that the product should be formulated as **17** rather than **18**. The formation of *N*-allyl compounds **17** may be explained to be formed *via* Claisen rearrangement which seems to be thermally induced under the condition of the reaction.

The products isolated herein were subjected to biological screening test. Research on this topic is currently in progress.



Scheme 4

This research was partially supported by the Research Council of the United Arab Emirates University and the International Organization for Chemical Sciences in Development (IOCD).

Experimental

Melting points were determined with a Mel-Temp melting point apparatus and are uncorrected. NMR spectra were recorded on a Nicolet NT 300, Bruker AC-250 and/or Varian EM-390 spectrometers. Chemical shifts are given in δ scale in part per million relative to tetramethylsilane as internal standard. Analytical TLC was performed using the ascending technique with EM silica gel 60 F_{254} precoated on plastic sheets. The IR spectra were obtained on Unicam SP 1025 spectrometer. A Hewlett-Packard 5995 Gas Chromatograph/Mass Spectrometer was used to record MS data at 70 eV. Elemental analyses were performed in the Chemistry Departments, Faculties of Science, Cairo, and Mansoura Universities and at M-H-W Laboratories, Phoenix, Arizona, U.S.A. The α-hydroxy-γ-ketoacids **3** needed for this work were prepared by following the previously established method [5, 11].

Dehydrative Cyclization of 1 (General Procedure)

A solution of **1** (4.7 mmol) in glacial acetic acid (5 ml), concentrated hydrochloric acid (3 ml) and water (3 ml) was

heated on a water-bath for 1h. The reaction mixture was poured onto crushed ice, the oily product was washed several times with water and the gummy material was recrystallized from benzene/petroleum ether.

5-Hydroxy-5-methyl-3-(2-phenylethyl)-2(5H)-furanone **4a**)

39.4%, *m.p.* 92–93 °C. – ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.60 (3H, s, CH_3), 2.57, 2.86 (4H, m, t, CH_2–CH_2), 4.32 (1H, s, OH), 6.69 (1H, t, =CH), 7.25 (5H, m, ArH). – ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 24.62, 26.47, 33.23, 104.71, 126.35, 128.42, 128.51, 134.80, 140.38, 148.09, 171.74.

$C_{13}H_{14}O_3$	Calcd.: C 71.54	H 6.46
(218.24)	Found: C 71.31	H 6.55

5-Hydroxy-5-methyl-3-[2-(4-methylphenyl)ethyl]-2(5H) furanone (4d)

47.5%, *m.p.* 96–97 °C. – ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.6 (3H, s, CH_3), 2.2 (3H, s, CH_3 Ar), 2.4, 2.6 (4H, 2×m, CH_2–CH_2), 3.22 (1H, br. s, OH), 7.2 (5H, m,=CH,ArH). – ^{13}C NMR (75.4 MHz, DMSO-d_6) δ: 20.94 (q), 24.55 (t), 28.51 (t), 32.70 (q), 104.00 (s), 128.00 (d), 129.00 (d), 134.83 (s), 135.80 (s), 137.14 (s), 147.41 (s), 171.00 (s).

$C_{14}H_{16}O_3$	Calcd.: C 72.38	H 6.94
(232.27)	Found: C 72.30	H 6.90

3-[2-(4-Chlorophenyl)ethyl]-5-hydroxy-5-methyl-2(5H)-furanone (**4e**)

80%; *m.p.* 127–129 °C. – IR ν_{max}(cm^{-1}): 3260, 1720, 1650. – ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.54 (3H, s, CH_3), 2.50, 2.84 (4H, 2×t, CH_2–CH_2), 7.07 (1H, s, OH), 7.26, 7.33 (4H, 2d, ArH), 7.38 (1H,s, = CH). – ^{13}C NMR (75.4 MHz, DMSO-d_6) δ : 24.93, 25.99, 32.04, 104.90, 128.22, 130.13, 130.77, 132.76, 139.67, 149.32, 171.80. – MS *m/z*(%): 254, 252 (3.41, 8.78) [M$^+$], 236, 234 (7.99, 21.44) [M$^+$ –H_2O], 157 (14.78), 129 (5.59), 128 (11.55), 127 (38.71).

$C_{13}H_{13}ClO_3$	Calcd.: C 61.80	H 5.20
(252.68)	Found: C 61.90	H 5.40

5-Acetoxy-5-methyl-3-(2-phenylethyl)-2(5H)-furanone (**5a**)

A solution of **4a** (0.049, 0.2 mmol) in acetic anhydride (2 ml) was heated on a steam-bath for 3 hrs. The reaction mixture was poured onto crushed ice, and the product was extracted from the mixture by benzene. The organic layer was dried over Na_2SO_4 and then evaporated. The yellowish oily residue was subjected to flash column chromatography on Silica gel using ethyl acetate as an eluent to give 5-acetoxy-5-methyl-3-(2-phenylethyl)-2(5*H*)-furanone (**5a**) as a pale yellow oil in 80% yield.– ^{1}H NMR (90 MHz, $CDCl_3$) δ: 1.72 (3H, s, CH_3), 2.0 (3H, s, CH_3), 2.79, 2.90 (4H, 2m, CH_2–CH_2), 6.90 (1H, s, =CH), 7.10 (5H, m, ArH).

$C_{15}H_{16}O_4$	Calcd.: C 69.21	H 6.20
(260.28)	Found: C 69.20	H 6.42

(±)- 4-Benzyl-3-hydroxy-5-(2-phenylethyl)-2(5H)-furanone (**6**)

A mixture of **4a** (0.1 g, 0.458 mmol) and 36% hydrochloric acid (2 ml) was heated on a steam-bath for 3 hrs. The reaction mixture was poured into crushed ice. The product that separated out was filtered off, dried and recrystallized from benzene/petroleum ether to give (±)-4-benzyl-3-hydroxy-5-(2-phenylethyl)-2(5*H*)- furanone (**6**) (52%) as colourless crystals, *m.p.* 115–117 °C (Lit. [5]: 118 °C). – ^{1}H NMR (250 MHz,$CDCl_3$) δ: 1.79 (1H, m, H-1'a), 2.15 (1H, m, H-1'b), 2.65 (2H, m, H-2'a,H-2'b) 3.43, 3.83 (2H, 2d J = 15.22 Hz; CH_2 of the benzyl group attached to position 4), 4.74 (1H, dd, J =2.97 and 8.23 Hz, H-5), 6.10 (1H, br. s, OH), 7.25 (10H, m, 2ArH). – ^{13}C NMR (62.5 MHz, $CDCl_3$) δ : 30.98, 34.74, 46.53, 80.34, 126.72, 127.54, 128.93, 129.04, 129.43, 129.87, 130.05, 133.69, 138.11, 140.99, 170.74; MS *m/z*(%): 294(2) [M$^+$], 292(99), 274(3), 262(6), 248(14), 217(6), 157(4), 145(2), 129(6), 115(6), 165(6), 91(100), 77(4), 65(4).

6-Aryl-4-(2-arylethyl)-2,3-dihydropyridazin-3-ones (7) (General Procedure)

Method A:

A mixture of **1** (6.5 mmol) in ethanol (10 ml), hydrazine hydrate (6 ml) and a few drops of glacial acetic acid was heated under reflux for 3 hrs. The product that separated out on concentration was filtered off, washed with ethanol and dried.

Method B:

A solution of **4** (3.7 mmol) in ethanol (10 ml) was refluxed with hydrazine hydrate (1 ml) on a water-bath for 2 hrs. The product was collected by filteration.

6-Phenyl-4-(2-phenylethyl)-2,3-dihydropyridazin-3-one (**7a**)

56% method A; *m.p.* 165–166 °C. – ^{1}H NMR (90 MHz, DMSO-d_6) δ: 3.00 (4H, s, CH_2–CH_2), 7.39, 7.66 (11 H, 2×m, ArH), 12.82 (1H, s, NH); MS *m/z*(%): 276 (56) [M$^+$], 275 (8), 259 (13), 128 (9), 91 (100); IR ν_{max} (cm^{-1}) : 3134, 1655.

$C_{18}H_{16}N_2O$	Calcd.: C 78.23	H 5.83	N 10.14
(276.33)	Found: C 77.90	H 5.80	N 9.96

6-(4-Methylphenyl)-4-(2-phenylethyl)-2,3-dihydropyridazin-3-one (**7b**)

75% method A; *m.p.* 158–159 °C. – ^{1}H NMR (90 MHz, DMSO-d_6) δ: 2.34 (3H, s, CH_3), 2.88 (4H, s, CH_2–CH_2), 7.28, 7.70 (10H, d, m, ArH), 13.02 (1H, s, NH); IR ν_{max}(cm^{-1}) : 3130, 1648.

$C_{19}H_{18}N_2O$	Calcd.: C 78.59	H 6.25	N 9.65
(290.35)	Found: C 78.30	H 6.40	N 9.60

6-(4-Methoxyphenyl)-4-(2-phenylethyl)-2,3-dihydropyridazinone (**7c**)

86% method A; *m.p.* 197 °C. – ^{1}H NMR (90 MHz, DMSO-d_6) δ: 2.85, 2.91 (4H, 2×m,CH_2–CH_2), 3.80 (3H, s, OCH_3), 7.03, 7.28, 7.76 (10 H, d, m, m, ArH), 13.01 (1H, s, NH). – MS *m/z*(%): 306 (9) [M+], 128 (3), 121 (100), 91 (6); IR ν_{max} (cm^{-1}): 3128, 1653.

$C_{19}H_{18}N_2O_2$	Calcd.: C 74.49	H 5.92	N 9.15
(306.35)	Found: C 74.20	H 6.20	N 8.90

6-Methyl-4-(2-phenylethyl)-2,3-dihydropyridazin-3-one (**7d**)

82% method A, 88% method B; *m.p.* 118–120 °C. – ^{1}H NMR (250 MHz, $CDCl_3$) δ: 2.25 (3H, s, CH_3), 2.90 (4H, m, CH_2–CH_2), 6.82 (1 H, s, H-5), 7.25 (5H, m, ArH), 11.78 (1H, s, NH); MS *m/z*(%): 214(26) [M$^+$], 91 (100), 77 (5), 65 (16).

$C_{13}H_{14}N_2O$	Calcd.: C 72.86	H 6.58	N 13.07
(214.26)	Found: C 73.02	H 6.80	N 13.19

6-Aryl-2-(4-bromophenyl)-4-hydroxy-4-(2-phenylethyl)-2,3,4,5-tetrahydropyridazin-3-ones (8) (General Procedure)

A solution of **1** (2.8 mmol) in ethanol (25 ml) was heated under reflux with a solution of 4-bromophenylhydrazine (2.8 mmol) in ethanol (25 ml) for 7 hrs. The product that separated out on cooling was filtered off, washed with ethanol and dried.

2-(4-Bromophenyl)-4-hydroxy-6-phenyl-4-(2-phenylethyl)-2,3,4,5-tetrahydro-pyridazin-3-one) (**8a**)

40%; *m.p.* 120–121 °C. – ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 2.04 (4H, m, CH_2–CH_2), 2.80 (2H, m, CH_2), 3.90 (1H, s, OH), 7.15, 7.65, 7.80 (14H, 3×m, ArH): – MS *m/z*(%): 450, 448 (20,19) [M$^+$], 432(12), 430(15), 346(91), 344(100), 317(22), 315(23); IR ν_{max}(cm^{-1}): 3374, 1668.

$C_{24}H_{21}Br\,N_2O_2$	Calcd.:	C 64.15	H 4.71	N 6.26
(449.34)	Found:	C 64.20	H 4.80	N 6.50

2-(4-Bromophenyl)-4-hydroxy-6-(2-methylphenyl)-4-(2-phenylethyl)-2,3,4,5-tetra-hydropyridazin-3-one (**8b**)

44%; *m.p.* 158–160 °C. – ^{1}H NMR (90 MHz, $CDCl_3$) δ: 2.30 (4H, m, CH_2–CH_2), 2.36 (3H, s, CH_3), 2.76 (2H, m, CH_2), 3.33 (1H, s, OH), 7.17, 7.38, 7.59 (13H, m, d, d, ArH). – IR ν_{max} (cm^{-1}): 3399, 1669.

$C_{25}H_{23}BrN_2O_2$	Calcd.:	C 64.80	H 5.00	N 6.05
(463.36)	Found:	C 62.70	H 4.80	N 6.00

6-Aryl-2-(4-bromophenyl)-4-(2-phenylethyl)-2,3-dihydropyridazin-3-ones (9) (General Procedure)

To a solution of **8** (2.5 mmol) in glacial acetic acid (15 ml) hydrochloric acid (10 ml) was added. The mixture was heated on a water bath for 0.5 hrs. After cooling the product was filtered off, washed with water and dried.

2-(4-Bromophenyl)-6-phenyl-4-(2-phenylethyl)-2,3-dihydropyridazin-3-one (**9a**)

78%; *m.p.* 142 °C. – ^{1}H NMR (90 MHz, $CDCl_3$) δ: 2.96 (4H, s, CH_2–CH_2), 7.18, 7.33, 7.61 (14H, s, m, m, ArH). – IR ν_{max}(cm^{-1}): 1655, 1620.

$C_{24}H_{19}Br\,N_2O$	Calcd.:	C 66.83	H 4.44	N 6.50
(431.32)	Found:	C 66.90	H 4.60	N 6.40

2-(4-Bromophenyl)-6-(4-methylphenyl)-4-(2-phenylethyl)-2,3-dihydropyridazin-3-one (**9b**)

73%; *m.p.* 119–120 °C. – ^{1}H NMR (90 MHz, $CDCl_3$) δ: 2.83 (3H, s, CH_3), 3.02 (4H, s, CH_2–CH_2), 7.13–7.61 (14H, m, ArH). – IR ν_{max}(cm^{-1}): 1660, 1624.

$C_{25}H_{21}Br\,N_2O$	Calcd.:	C 67.42	H 4.75	N 6.29
(445.35)	Found:	C 67.50	H 4.50	N 6.30

6-Aryl-3-chloro-4-(2-phenylethyl)pyridazines (11) (General Procedure)

A mixture of **7** (7.5 mmol) and phosphoryl chloride (10 ml) was heated under reflux for 2 hrs. After cooling, the mixture was poured onto crushed ice. The mixture was neutralized with a saturated aqueous $NaHCO_3$ solution, and the resulting precipitate was filtered off, washed with water and dried. Yields and physical data are summarized in Table 1.

Table 1 Physical Data of 6-Aryl-3-chloro-4-(2-phenylethyl)-pyridazines (**11a–c**)

No.	Yield %	*m.p.* °C	Mol. Form. (Mol. wt.) [a]	^{1}H NMR [b] δ (ppm)	MS *m/z*(%)
11a	70	104	$C_{18}H_{15}ClN_2$ (294.77)	3.20 (s, 4H), 7.75 (m, 11H)	296(41), 94(100) [M$^+$], 25(11), 139(44), 102(31), 91(99)
11b	71	134–135	$C_{19}H_{17}ClN_2$ (308.80)	2.39 (s, 3H) 3.03 (s, 4H); 7.26 (s, 5H); 7.34 (d, 2H); 7.99 (d, 2H); 8.13 (s, 1H)	310(13), 308(36) [M$^+$], 273(4) 115(8), 91(100)
11c	71	110	$C_{19}H_{17}ClN_2O$ (324.80)	3.43 (s, 4H); 3.78 (s, 3H); 6.97 (d, 2H); 7.23 (s, 5H); 7.65 (d, 2H); 7.67 (s, 1H).	326(10), 324(31) [M$^+$], 91(100)

[a] Satisfactory microanalyses were obtained of all compounds.
[b] in $CDCl_3$

6-Aryl-8-(2-phenylethyl)-2,3-dihydro-*s*-triazolo[4,3-*b*]pyridazin-3-ones (12) (General Procedure)

A mixture of **11** (2.5 mmol), semicarbazide hydrochloride (2.5 mmol), 75 % aqueous ethanol (40 ml) and a few drops of hydrochloric acid was heated under reflux for 18 hrs. The reaction mixture was concentrated and the product was filtered off, washed with ethanol and dried. Yields and physical data are summarized in Table 2.

3-Benzyl-8-(2-phenylethyl)-6-phenyl-s-triazolo[4,3-b] pyridazine (**13**)

A mixture of **11** (1.17g, 4mmol), phenylacetylhydrazine (0.6 g, 4 mmol), and n-butanol (10 ml) was refluxed for 8 hrs. The

Table 2 Physical Data of 6-Aryl-8-(2-phenylethyl)-2,3-dihydro-*s*-triazolo[4,3-*b*]pyridazin-3-ones(**12a-c**)

No.	Yield %	m.p. °C	Mol. Form. (Mol. wt.) [a]	IR(KBr) ν (cm^{-1}) OCN NH	^{1}H-NMR($CDCl_3$) δ (ppm)
12a	80	163–165	$C_{19}H_{16}N_4O$ (316.35)	1662 3129	2.87 (s, 4H), 7.23 (s, 5H), 7.41 (m, 3H), 7.79 (m, 3H), 13.00 (s,1H, D_2O-exchangable)
12b	84	175	$C_{20}H_{18}N_4O$ (330.37)	1656 3135	2.35 (s, 3H), 2.87 (s, 4H), 7.23 (m, 6H), 7.67 (m, 4H),12.96 (s,1H D_2O-exch.)
12c	68	199–200	$C_{20}H_{18}N_4O_2$ (346.37)	1653 3135	2.83 (s, 4H), 3.74 (s, 3H), 6.91 (d, 2H), 7.18 (s, 5H), 7.60 (s, 1H), 7.66 (d, 2H),12.73 (s, 1H D_2O-exch.)

[a] Satisfactory microanalyses were obtained of all compounds.

product was separated out on concentration, was collected by filtration, dried and crystallized from ethanol–water to give **13** (1.029g. 66%); *m.p.* 230–232 °C, R_f 0.77 (EtOAc-*n*-hexane 1:1). – ^{1}H NMR (90 MHz, $CDCl_3$) δ: 3.25 (4H, m, CH_2–CH_2), 4.5 (2H, s, CH_2), 6.92 (1H, s, H-7), 7.18, 7.35, 7.62 (15H, 3m, ArH).

$C_{26}H_{22}N_4$	Calcd.	C 79.97	H 5.68	N 14.34
(390.47)	Found	C 80.12	H 5.77	N 14.27

6-Aryl-8-(2-phenylethyl)tetrazolo[1,5-b]pyridazines (15) (General Procedure)

A solution of **11** (3.0 mmol) and sodium azide (3.3 mmol) in *N,N*-dimethyl formamide (45 ml) was heated under reflux for 8 hrs. It was then cooled, and poured into water (200 ml). The product that separated out was filtered off, washed with water and dried.

6-Phenyl-8-(2-phenylethyl)tetrazolo[1,5-b]pyridazine (**15a**)

59%; *m.p.* 249 °C. – IR ν_{max} (cm^{-1}): 2924, 1611.

$C_{18}H_{15}N_5$	Calcd.: C 71.74	H 5.02	N 23.24
(301.34)	Found: C 72.00	H 5.12	N 23.54

6-(4-Methylphenyl)-8-(2-phenylethyl)tetrazolo[1,5-b] pyridazine (**15b**)

59%; *m.p.* 150 °C. – IR ν_{max}(cm^{-1}): 2925, 1631.

$C_{19}H_{17}N_5$	Calcd. C 72.36	H 5.43	N 22.21
(315.37)	Found C 72.10	H 5.31	N 22.00

6-(4-Methoxyphenyl)-8-(2-phenylethyl)tetrazolo[1,5-b]pyridazine (**15c**)

61; *m.p.* 110 °C. – IR ν_{max}(cm^{-1}): 2926, 1611.

$C_{19}H_{17}N_5O$	Calcd.: C 68.86	H 5.17	N 21.14
(331.37)	Found C 69.00	H 5.30	N 21.30

2-Allyl-6-aryl-4-(2-phenylethyl)pyridazin-3-ones (17) (General Procedure)

Compound **11** (3.4 mmol) was added to a solution of sodium (10 mmol) in allyl alcohol) (30 ml), and the mixture was heated under reflux for 18 hrs. The reaction mixture was poured into water (50 ml), and the precipitate was filtered off, washed with water and dried.

2-Allyl-6-phenyl-4-(2-phenylethyl)pyridazin-3-one (**17a**)

58%; *m.p.* 62–63 °C. – ^{1}H NMR (90 MHz, DMSO-d_6) δ: 2.96 (4H, s, CH_2–CH_2), 5.01 (2H, d, CH_2), 5.32 (2H, m, =CH_2), 5.63 (1H, m, –CH=), 7.28, 7.90 (11H, 2×m, ArH); MS *m/z*(%): 316(4) [M^+], 315 (18), 313 (14), 301 (11), 289 (23), 276 (23), 141 (33), 91 (100). – IR ν_{max} (cm^{-1}): 2934, 1649, 1605.

$C_{21}H_{20}N_2O$	Calcd.: C 79.72	H 6.37	N 8.86
(316.39)	Found: C 79.80	H 6.37	N 8.70

2-Allyl-6-(4-methylphenyl)-4-(2-phenylethyl)pyridazin-3-one (**17b**)

52%; *m.p.* 60–61 °C. – ^{1}H NMR (90 MHz, DMSO-d_6) δ: 2.35 (3H, s, CH_3), 2.94 (4H, s, CH_2–CH_2), 4.99 (2H, d, CH_2), 5.28 (2H,m, =CH_2), 6.11 (1H, m, –CH =), 7.25, 7.87 (10H, 2×m, ArH); MS *m/z*(%): 330 (99) [M^+], 329 (54), 276 (48), 141 (69), 91 (100). – IR ν_{max} (cm^{-1}): 2949, 1649, 1604.

$C_{22}H_{22}N_2O$	Calcd. C 79.97	H 6.71	N 8.48
(330.42)	Found C 79.90	H 6.70	N 8.50

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