An unexpected valence bond isomerization to the heteroaromatic ring system: [1,2,3]triazolo[4,5-*d*]pyridazine

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The arylazo substituted salt 2 when treated with a base underwent a valence bond isomerization to yield a derivative of the heteroaromatic ring system, [1,2,3]triazolo[4,5-*d*]pyridazine (4).

Recently we have elaborated an easy synthetic pathway to some tricyclic zwitterionic fused pyridazo[1,2,4]triazines[1] (*e.g.* **1**) and have shown that these compounds readily undergo cycloadditions as well as Michael additions.[2] As a continuation of these studies the reactivity of the new zwitterions towards diazonium salts seemed of particular interest.

When the zwitterion **1** was treated with aryldiazonium salts at rt, the change of colour from green to bright red indicated that an azo coupling had taken place. Work-up of the reaction mixture led to the isolation of the stable brilliant red crystalline fluoroborate salt **2**.[3] This salt when treated with a base was converted into the neutral azo compound which decomposed upon storage at rt and a yellow component, as shown by tlc, appeared gradually. This decomposition could be accelerated by heating the suspension of **2** in toluene for a few minutes: a yellow crystalline substance was then formed in good yield. For the structure of this yellow compound the *peri* fused **3** was first anticipated. This could be easily rationalized by assuming attachment to the negatively and positively polarized nitrogen atoms (1,5-dipolar cyclization or 'pseudo-electrocyclization'[4]). Upon observation of some further transformations, however, this conclusion seemed ambiguous and structure **4** (*i.e.* a product of a possible thermal electrocycloreversion of **3**) had to be considered.[5] The ring closure (which might proceed *via* the intermediate *peri*-fused tetracycle **3**, or could also be formed from **2** in one single step) seems to represent a special case of a ring closure to [1,2,3]triazole starting from an azo compound.[6]

Comparison of the heats of formation of **3** (208.0 kcal mol^{-1}) and **4** (164.2 kcal mol^{-1}), calculated for a derivative unsubstituted at the triazole ring by the semiempirical PM3 method,[7] also revealed that the ring-opened form **4** is energetically more favourable (by 44 kcal mol^{-1}). A final decision on this structural problem was provided by an X-ray analysis of the product obtained from **2b** which showed that the isolated compound has in fact the ring-opened structure **4b**, as shown in Fig. 1.

The X-ray analytical data revealed that the bond distances and angles are normal.[8] The endocyclic bond angle at N2 is 116.2(2)°, at N1 and N3 102.5(2) and 102.7(2)°. The bond distances N1–N2 and N2–N3 are 1.336(2) and 1.345(2) Å, shorter than N5–N6 (1.364(2) Å).

The whole molecule is basically planar, with the exception of the pyridine moiety which is perpendicular to the mean molecular plane. A characteristic feature of the crystal packing is the infinite stacking with strong π ring interactions. The centroids of the nirophenyl ring at (*x*,*y*,*z*) and the pyridazine ring at (1 + *x*,*y*,*z*) are 3.52 Å apart (the dihedral angle is 0.81°).[9]

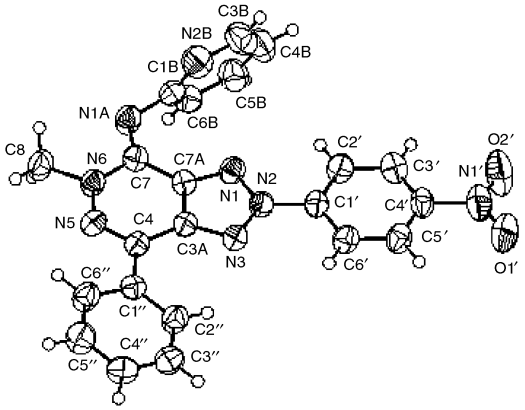
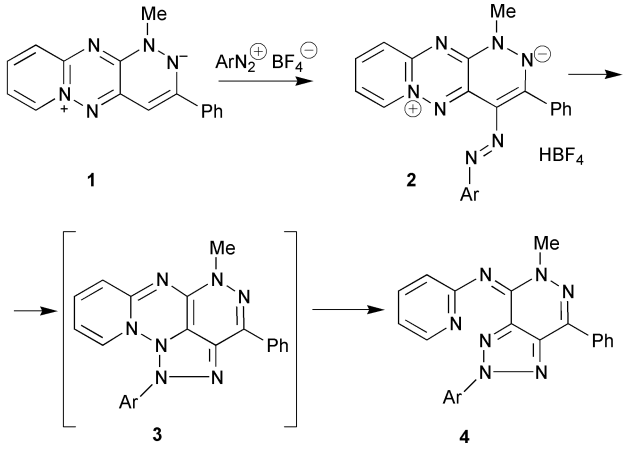
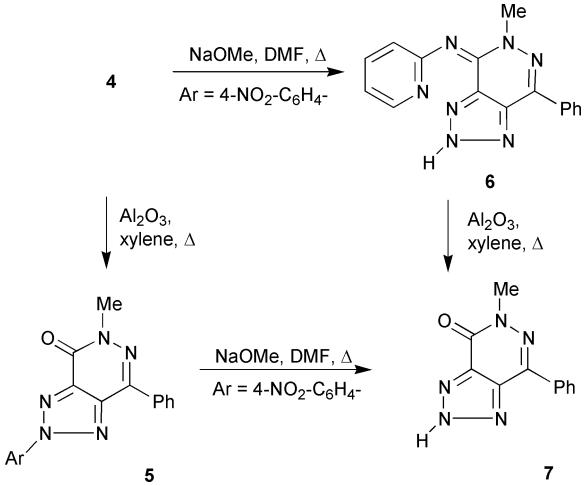


Fig. 1 A molecular diagram[9] of **4b** with the numbering of atoms. Anisotropic displacement parameters represent 50% probabilities.



Scheme 1 (a) Ar = 4-ClC_6H_4–, (b) Ar = 4-$NO_2C_6H_4$–, (c) Ar = 4-$CH_3OC_6H_4$–.



Scheme 2

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The Schiff base side-chain of **4** easily underwent hydrolysis in the presence of alumina at higher temperature (*i.e.* in boiling xylene) and gave rise to the triazolopyridazinone **5**,[10] a derivative of the heteroaromatic [1,2,3]triazolo[4,5-*d*]pyridazine ring system (saturated[11] and unsaturated derivatives[12,13] of this ring skeleton have been described elsewhere).

The 4-nitrophenyl substituted compounds (*i.e.* **4b** and **5b**) proved to be suitable for transformations to the derivatives containing an unsubstituted triazole moiety. Thus, these compounds when treated with sodium methylate in DMF underwent an *ipso* substitution and afforded the dearylated products **6**[14] and **7**.[15]

Our results reveal that this observed valence bond isomerization provides an easy access to a hitherto unexplored area of triazolopyridazines.

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Notes and references

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3 **2a**: mp 228–230 °C (95 %); **2b**: mp 269–271 °C (67%); **2c**: 234–236 °C (95%). *Selected spectroscopic data for* **2b**: ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.8 (3H, s, 1-Me), 7.2–7.9 (7H, m, Ar), 8.1–8.25 (5H, m, Ph), 9.4 (1H, d, J = 7 Hz, 7-H), 13.0 (1H, s, 2-NH).

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5 **4a**: mp 225–227 °C (74%); **4b**: mp 269–271 °C (67%); **4c**: 226–228 °C (70%). *Selected spectroscopic data for* **4b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.07 (3H, s, 5-Me), 7.01 (1H, m, J = 8, 1, 1 Hz, 3′-Py), 7.13 (1H, m, J = 7, 5, 1 Hz, 5′-Py), 7.47 (1H, m, Ph), 7.53 (2H, m, Ph), 7.74 (1H, m, J = 7, 8, 2 Hz, 4′-Py), 8.05 (2H, m, Ar), 8.32 (2H, m, Ph), 8.34 (2H, m, Ar), 8.47 (1H, m, J = 5, 2 , 1 Hz, 6′-Py); ^{13}C NMR ($CDCl_3$): δ 42.1, 116.6, 118.6, 120.5, 125.1, 127.1, 128.6, 129.6, 133.1, 135.1, 137.8, 138.57, 141.8, 142.9, 144.6, 147.6, 148.7, 162.4; MS, M_{calcd}: 424.1396, M_{found}: 424.1390 ± 5 ppm.

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8 *Crystal data for* **4b**: $C_{22}H_{16}N_8O_2$, M = 424.43, monoclinic, a = 6.163(1), b = 17.243(4), c = 18.471(1) Å, β = 92.00(1)°, U = 1961.7(6) Å^3, T = 293(2) K, space group $P2_1/c$ (No. 14), Z = 4, μ(Mo-Kα) = 0.099 mm^{-1}, 4175 reflections measured, 3713 unique (R_{int} = 0.0206) which were used in all calculations. The final *wR*2 was 0.1036 (all data).

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10 *Selected spectroscopic data for* **5b** : yellow crystals, mp 262–264 °C (86%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.87 (3H, s, Me), 7.56–7.64 (3H, m, Ph), 8.34 (2H, m, Ar), 8.52 (2H, m, Ar), 8.58 (2H, m, Ph); Calc. for: $C_{17}H_{12}N_6O_3$, C, 58.62; H, 3.45; N, 24.14. Found: C, 58.56; H, 3.51; N, 24.06%.

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14 *Selected spectroscopic data for* **6**: Pale yellow crystals, mp 260 °C (70%); ^{1}H NMR (400 MHz**,** DMSO-d_6): δ 4.18 (3H, s, 5-Me), 7.15 (1H, m, J = 7, 5, 1 Hz, 5′-Py), 7.4 (1H, m, J = 8, 1, 1 Hz, 3′-Py), 7.55–7.6 (3H, m, Ph), 7.99 (1H, m, J = 8, 7, 2 Hz, 4′-Py), 8.21 (1H, m, J = 5, 2, 1 Hz, 6′-Py), 8.65 (2H, m, Ph), 14.6 (1H, b, 5-NH); MS, M_{calcd}: 303.1232, M_{found}: 303.1233 ± 5 ppm.

15 *Selected spectroscopic data for* **7**: white crystals, mp 245–246 °C (70%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.82 (3H, s, 5-Me), 7.5–7.6 (3H, m, Ph), 8.3 (2H, m, Ph); MS, M_{calcd}: 227.0807, M_{found}: 227.0808 ± 5 ppm.