Unexpected Transformations of 4-Azido-2-(2′-hydroxyphenyl)-5-ethoxycarbonylpyrimidine: the Formation of 4-Hydroxyamino-2-(2′-hydroxyphenyl)-5-ethoxycarbonylpyrimidine and Ethyl 3-(2′-Hydroxybenzoylamino)-2-(1″*H*-tetrazol-5″-yl)acrylate

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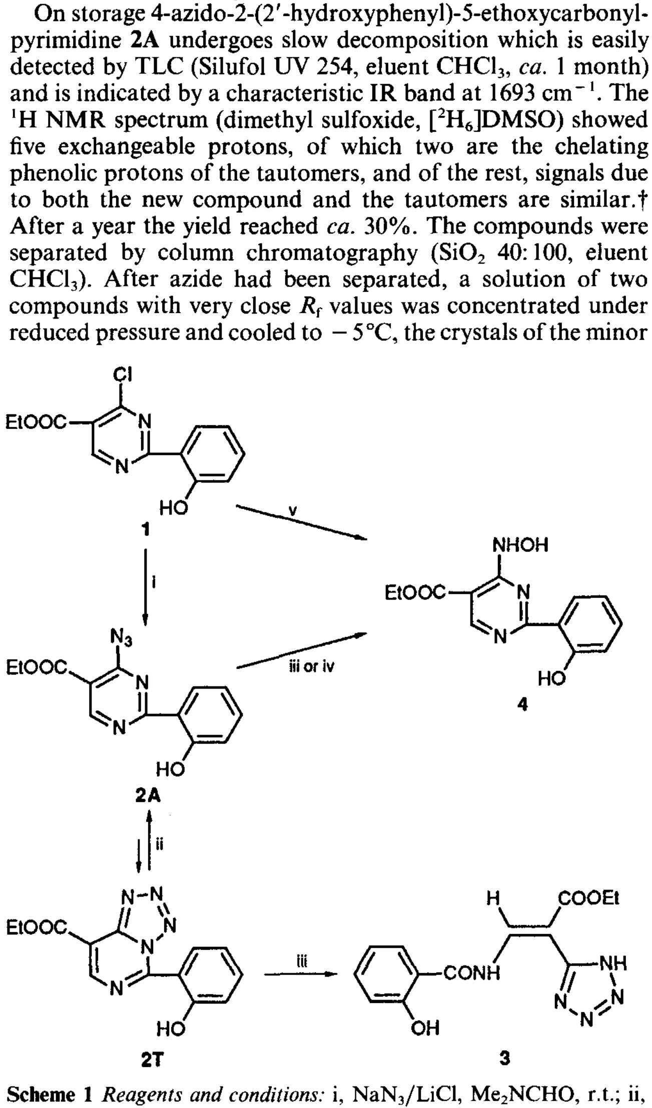
The title compound undergoes a spontaneous solid-phase transformation in the dark into **3** and **4** at room temperature. On refluxing azide **2A** in water, the hydroxylamine **4** was afforded in good yield.

In continuation of our studies on the azido–tetrazole tautomerism of azidopyrimidines and their use as light-sensitive compounds in photoimaging compositions,[1] we report an unusual spontaneous solid-phase transformation in the dark of azide **2A** at room temperature (r.t.).

On storage 4-azido-2-(2′-hydroxyphenyl)-5-ethoxycarbonylpyrimidine **2A** undergoes slow decomposition which is easily detected by TLC (Silufol UV 254, eluent $CHCl_3$, *ca.* 1 month) and is indicated by a characteristic IR band at 1693 cm^{-1}. The ^1H NMR spectrum (dimethyl sulfoxide, $[^2H_6]$DMSO) showed five exchangeable protons, of which two are the chelating phenolic protons of the tautomers, and of the rest, signals due to both the new compound and the tautomers are similar.† After a year the yield reached *ca.* 30%. The compounds were separated by column chromatography (SiO_2 40:100, eluent $CHCl_3$). After azide had been separated, a solution of two compounds with very close R_f values was concentrated under reduced pressure and cooled to − 5 °C, the crystals of the minor product (*ca.* 1%) were collected and the solvent was removed to give the main compound.‡

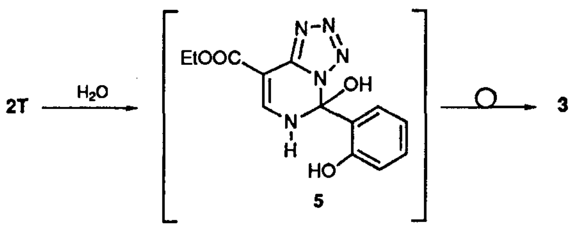


Scheme 1 *Reagents and conditions:* i, NaN_3/LiCl, Me_2NCHO, r.t.; ii, **2A**/**2T** ratio, *ca.* 22 °C: 100:0 in $CDCl_3$, 59:41 in $[^2H_6]$DMSO; iii, solid state, storage, r.t., atmospheric moisture; iv, H_2O, reflux, *ca.* 3 h; v, NH_2OH, EtOH, 0–3 °C, *ca.* 1 h

The high-resolution mass spectrum (HRMS) of the molecular ion for the minor compound was consistent with the formula $C_{13}H_{13}N_5O_4$, corresponding to addition of one molecule of water to the nucleus of **2**. The structure of **3** was assigned to this molecule on the basis of spectral data (IR, ^1H and ^{13}C NMR). The formation of ethyl 3-(2′-hydroxybenzoylamino)-2-(1″*H*-tetrazol-5″-yl)acrylate **3** may be explained by the presence of a small amount of tautomer **2T**, which undergoes covalent hydration[2] followed by isomerization of an unstable intermediate **5** into an open form **3** (Scheme 2).§

As a result, the side-chain configuration of acrylate **3** corresponds to that given by the structural formula in Scheme 1. This stereochemistry is also supported by experimental values of vicinal C,H spin coupling[3] in **3**, *i.e.* ${}^3J^{trans}_{C^{5''}\text{-}H^3} = 10.7$ Hz > ${}^3J^{cis}_{C^1\text{-}H^3} = 4.9$ Hz.

The HRMS of the main compound provided the molecular formula $C_{13}H_{13}N_3O_4$, which corresponds to the loss of N_2 and addition of H_2O by the molecule of **2**. Spectral data (^1H, ^{13}C, ^{15}N NMR, IR, UV) of this compound agree with structure **4**, 4-hydroxyamino-2-(2′-hydroxyphenyl)-5-ethoxycarbonylpyrimidine. The identity was confirmed by comparison with an authentic sample prepared by interaction of **1** with NH_2OH



Scheme 2

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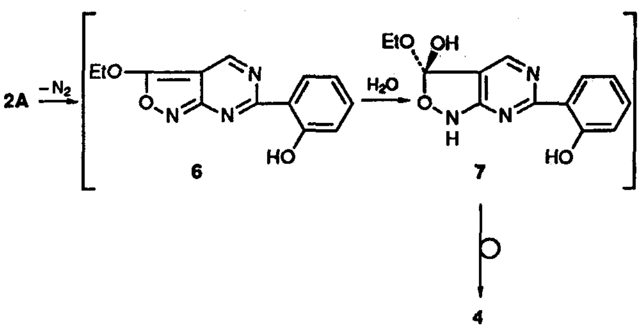
† *General experimental details.* All NMR spectra were recorded on a Bruker AC-200 or AM-400 spectrometer. ^1H and ^{13}C NMR chemical shifts are given relative to $[^2H_6]$DMSO using resonances at 2.50 and 39.50 ppm as an internal reference, respectively, while ^{15}N NMR spectra are referenced externally to the nitrogen resonance of 90% formamide (δ 112.4), referred to liquid NH_3 in $[^2H_6]$DMSO. All coupling constant values *J* were measured to an accuracy of ± 0.25 Hz.

‡ Characterization data for **2**: m.p. *ca.* 125 °C (decomp.); IR (KBr) ν/cm^{-1} 2138 s (N_3), 1732 s (CO); ^1H NMR (200.13 MHz) data for **2A**: in $CDCl_3$ δ 1.39 (t, 3H, Me), 4.38 (q, 2H, $CHCH_2$), 6.96 (m, 2H, 3′-H and 5′-H), 7.41 (m, 1H, 4′-H), 8.35 (dd, 1H, 6′-H), 9.01 (s, 1H, 6-H), 12.80 (s, 1H, 2′-OH); in $[^2H_6]$DMSO δ 1.33 (t, 3H, Me), 4.33 (q, 2H, CH_2), 6.96–7.18 (m, 3′-H and 5′-H), 7.51 (m, 1H, 4′-H), 8.34 (m, 1H, 6′-H), 9.17 (s, 1H, 6-H), 12.88 (s, 1H, 2′-OH); for **2T**: in $[^2H_6]$DMSO δ 1.41 (t, 3H, Me), 4.50 (q, 2H, CH_2), 6.96–7.18 (m, 3′-H and 5′-H), 7.60 (m, 1H, 4′-H), 8.11 (dd, 1H, 6′-H), 9.06 (s, 1H, 7-H), 11.17 (s, 1H, 2′-OH).

§ **3**: m.p. 265–268 °C; ^1H NMR (200.13 MHz, $[^2H_6]$DMSO, 30 °C) δ 1.33 (t, 3H, Me), 4.36 (q, 2H, CH_2), 7.00 (m, 1H, 5′-H), 7.10 (dm, 1H, 3′-H), 7.51 (m, 1H, 4′-H), 8.00 (dd, 1H, 6′-H), 8.81 (br d, 1H, 3-H), 12.00 (br d, 1H, NH), 12.88 (br s, 1H, OH, the 1″-NH proton was not observed); ^{13}C NMR (100.61 MHz, $[^2H_6]$DMSO, 30 °C) δ 14.14 (CH_3), 61.03 (CH_2, ${}^1J_{CH}$ 148.5 Hz), 94.70 (C-2, ${}^2J_{C^2\text{-}H^3}$ 2.2 Hz), 116.34 (C-1′), 117.06 (C-3′), 119.75 (C-5′), 131.66 (C-6′), 135.22 (C-4′), 139.94 (C-3, ${}^1J_{CH}$ 176.2 Hz), 149.68 (C-5″, ${}^3J_{C^{5''}\text{-}H^3}$ 10.7 Hz), 157.57 (C-2′), 163.94 (CON, ${}^3J_{C\text{-}H^3}$ ${}^3J_{C\text{-}H^{6'}}$ 4.2, ${}^4J_{C\text{-}H^{3'}}$ 1.2 Hz), 164.64 (C-1, ${}^3J_{C^1\text{-}H^3}$ 4.9, ${}^3J_{C^1\text{-}H(CH_2)}$ 3.5 Hz); IR (KBr) ν/cm^{-1} 3212 br, 1696 (CO), 1672 (CO), 1604, 1464, 1400, 1282, 1214, 1104, 1064, 1026, 756; HRMS *m/z* (M^+) Found: 303.0969. (Calc. for $C_{13}H_{13}N_5O_4$: 303.0967).



Scheme 3

(Scheme 1) by analogy with ref. 4. In our opinion, such a conversion of the azido group into the hydroxyamino radical residue is a consequence of successive chemical reactions of tautomer **2A** (Scheme 3).¶ It is likely that the transformation is initiated by azide cyclization onto an adjacent ester grouping[5] to give the isoxazole **6** with concomitant loss of N_2 which undergoes nucleophilic attack of the H_2O molecule at C-3 followed by isomerization of intermediate **7** to the open-chain form **4**. This process also takes place on refluxing a suspension of azide **2A** in water (Scheme 1).

Further investigations on the thermal behaviour of azide **2A** in both the solid state and in solution are now in progress.

¶ **4**: yellow crystals (from benzene), m.p. 182–184°C; ^1H NMR (400.13 MHz, [$^2H_6$]DMSO, 30°C) δ 1.33 (t, 3H, Me), 4.33 (q, 2H, CH_2), 6.93 (m, 2H, 3′-H and 5′-H), 7.43 (m, 1H, 4′-H), 8.39 (dd, 1H, 6′-H), 8.84 (c, 1H, 6-H), 9.80 (br s, 1H, NH), 10.58 (br s, 1H, OH), 11.65 (s, 1H, 2′-OH, shifting in time to 13.97); ^{13}C NMR (100.61 MHz, [$^2H_6$]DMSO, 30°C) δ 14.02 (CH_3), 60.97 (CH_2, $^1J_{CH}$ 148.7 Hz), 101.07 (C-5, $^2J_{C^5\text{-}H^6}$ 6.2 Hz), 117.76 (C-3′), 117.95 (C-1′), 118.55 (C-5′), 129.42 (C-6′), 133.87 (C-4′), 157.82 (C-6, $^1J_{C^6\text{-}H^6}$ 183.4 Hz), 158.34 (C-4), 161.11 (C-2′), 164.28 (C=O, $^3J_{C(O)\text{-}H^6}$ 3.2, $^3J_{C(O)\text{-}H(CH_2)}$ 3.2 Hz), 165.77 (C-2, $^3J_{C^2\text{-}H^6}$ 11.4, $^3J_{C^2\text{-}H^{6'}}$ 4.3 Hz); ^{15}N NMR (40.53 MHz, [$^2H_6$]DMSO, 30°C) δ 149.91 (NH, $^1J_{NH}$ 108.3 Hz), 217.75 (N-3), 243.88 (N-1, $^2J_{N^1\text{-}H^6}$ 10.8 Hz); IR (KBr) ν/cm^{-1} 3315 br, 1693 (CO), 1607, 1570, 1454, 1394, 1275, 1227, 1161, 762; UV λ_{max}/nm (lg ε) ($CHCl_3$) 278 (4.24), 354 (4.09); HRMS m/z (M^+) Found: 275.0909. (Calc. for $C_{13}H_{13}N_3O_4$: 275.0906).

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Received: Moscow, 17th November 1992
Cambridge, 14th December 1992; Com. 2/06247J