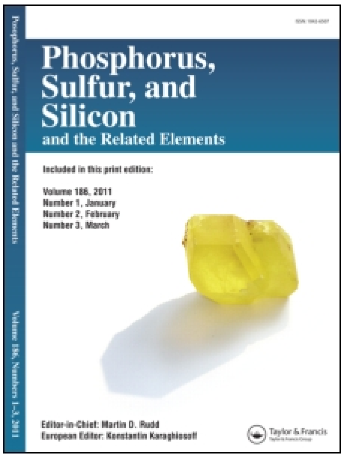

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SUSCEPTIBILITY OF 2-ARYLIDENE-3,5.DIARYL-2,3-DIHYDRO-1,3, 4-THIADIAZOLES TO HYDROLYSIS

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(Z)-2-Benzylidene-2,3-dihydro-3,5-diphenyl-1,3,4-thiadiazole (**1 a**) undergoes slow hydrolysis during long term storage (*ca* eleven years) to *N'*-phenacetyl-*N'*-phenyl-*N*-thiobenzhydrazide (**2a**); the 2-(4-methoxybenzylidene) derivative behaves similarly.

Keywords: 1,3,4-Thiadiazoles; methine bases; hydrolysis; NMR spectra

As part of a recent ^{13}C-NMR study,[1] we examined compounds **1 a-f**[2] which had been stored as pure samples in screw-capped vials at room temperature in the dark for some eleven years. We noted that the melting points of the samples stored as **1a** and **1b** (designated as **A** and **B**, respectively) had changed, while **1 c-f** remained the same. We now report spectroscopic evidence that shows that **1 a** and **1b** underwent hydrolysis during storage to **2 a** and **2b**, respectively.

Sample **A** was first recrystallized. The ^{13}C-NMR spectrum (DMSO-d_6) of the purified sample showed signals expected for compound **2 a**, with the CH_2 carbon signal detectable as a slight asymmetry in the DMSO-d_6 septet. This signal was apparent in pyridine-d_5 (δ 41.9) and in acetonitrile-d_3 (δ 41.1). The ^{1}H-NMR spectrum (DMSO-d_6) at 300 K showed signals for CH_2 (2 H), aromatic protons (15 H) and NH (1 H), plus a minor signal at δ 3.31 (s) which we attribute to CH_2 protons in a small amount of the anion of **2a** present in the relatively basic solvent.[3] The NH signals appeared as two singlets (peak ratio for downfield:upfield signals was 79:21) and the

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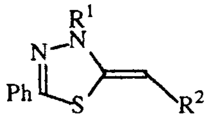

1

$PhCSNHNPhCOCH_2R$

2

a $R^1 = R^2 = Ph$
b $R^1 = Ph$, $R^2 = C_6H_4OMe$ (4)
c $R^1 = Ph$, $R^2 = C_6H_4NO_2$ (4)
d $R^1 = C_6H_3Br_2$ (2,4), $R^2 = Ph$
e $R^1 = C_6H_3Br_2$ (2,4), $R^2 = C_6H_4OMe$ (4)
f $R^1 = C_6H_3Br_2$ (2,4), $R^2 = C_6H_4NO_2$ (4)

CH_2 signals as a downfield AB system plus an upfield broad singlet (peak ratio for downfield:upfield signals was 78:22), each of which coalesced to broad singlets as the temperature was raised to 340 K. Lowering the temperature to 300 K restored the original spectrum. This is consistent with a slow exchange between two conformers of **2 a,** in one of which the CH_2 protons are diastereotopic. The system is fluxional and the observed diastereotopicity can be attributed to restricted rotation. The FAB mass spectrum also supports formula **2 a.**

The FAB mass spectrum of **B** (insufficient for purification) showed *m/z* 377 (MH^+), indicating **2b** as the structure of the transformation product of **1 b.** The ^{13}C-NMR spectrum (DMSO-d_6) showed that **B** was a mixture of **1b** and **2b,** though no signal could be assigned with certainty for the C=S carbon of **2b.** The CH_2 carbon signal of **2b** was detected at δ 38.8 by a DEPT experiment. The ^1H-NMR spectrum (DMSO-d_6) confirmed that the sample was mainly **2 b,** but contained *ca* 12% of **1 b**(based on peak integrations of the methine H of **1 b** and NH of **2b** relative to total aromatic protons). The ^1H-NMR spectrum showed that **2b,** like **2 a,** equilibrated between two species with the major one displaying CH_2 protons as a downfield AB system.

It is apparent that 2-arylidene-3,5-diaryl-2,3-dihydro-1,3,4-thiadiazoles should be viewed as susceptible to hydrolysis, and, for storage beyond short term, dry, sealed ampoules are recommended. Hydrolysis might occasionally be useful for the preparation of *N'*-aracetyl-*N'*-aryl-*N*-thiobenzhydrazides,[2] but steric and resonance effects are likely to lead to individual differences between compounds. For example, an aryl group at N3 sited perpendicular to the thiadiazole ring, as in **1 d-f**, impedes approach of a water molecule to C2 via the π-system, while extended electron delocalisation, as in **1 c** and **1f**, depresses reactivity at C2.

EXPERIMENTAL

The IR spectrum was obtained using an Analect FX 6260 FT IR spectrophotometer. ^{13}C and ^{1}H-NMR Spectra were run on a Bruker Avance DPX 300 FT NMR spectrometer in DMSO-d_6 at 75 MHz and 300 MHz, respectively, at 300 K unless otherwise stated. Chemical shifts are reported in ppm downfield from tetramethylsilane. FAB mass spectra were acquired for samples in 3-nitrobenzyl alcohol matrices bombarded with Xe (atom gun at 1ma/7.5 kV) using a Kratos Concept 1S double focussing mass spectrometer interfaced to Kratos DART acquisition system controlled by a Sun Sparcstation with Kratos XMach3 software. The *m/z* values are for the lowest isotopic species, with relative intensities in parentheses.

The transformation product of 1a

The original sample of **1a** had a mp 121–124 °C,[2] later independently confirmed.[1,4] When reexamined, this sample (**A**) had a mp 160–162 °C. Crystallization from nitromethane gave **2 a** as yellow platelets, mp 174–175 °C; IR (KBr) 3160br (NH of -NHCS-), 1655s (amide C=O) and 1220s (C=S of -NHCS-) cm^{-1} ;^{13}C-NMR δ 124.8, 127.0, 127.5, 128.5, 129.1, 129.3, 130.6, 132.7, 135.6, 139.3, 140.8 (arom C), 171.7 (C=O) and 199.9 (C=S); ^{1}H-NMR δ 3.31 (s), 3.66 (s), 3.75 (d, J=16.2 Hz, H_A of AB system), 3.94 (d, J= 16.2 Hz, H_B of AB system), 6.85–8.20 (m, arom H), 12.51 (s, NH) and 12.96 (s, NH) [at 340 K, the minor signal at δ 3.31 shifts to 3.14 (s), the CH_2 signal appears at δ 3.81(br s) and the NH signal at δ

12.72 (br s)]; FAB mass spectrum *m/z* 347 (MH^+, 45), 329 (15), 255 (39), 194 (24), 121 (71), 105 (29), 104 (34) and 91 (100%).

The transformation product of 1b

The original sample of **1b** had a mp 91–93 °C, 109–110 °C (double mp).[2] When reexamined, this sample (**B**) had a mp 122–124 °C, 129–132 °C (double mp); FAB mass spectrum *m/z* 377 (MH^+, 38), 359 (35), 358 (23), 255 (31), 225 (14), 135 (24), and 121 (100). The ^{13}C-NMR spectrum revealed **B** to be a mixture of **1 b** and **2 b**. Two signals appeared at δ 54.96 and 55.02 (CH_3), one at 91.7 (methine carbon of **1 b**), with a total of 24 signals between 113.6 and 158.0 which included two at 156.2 and 158.0 (arom C), and one at 170.9 (C=O of **2b**). The ^{1}H-NMR spectrum confirmed that **B** was a mixture of **1b** and **2b.** The presence of **1 b** is verified by signals at δ 3.74 (CH_3) and 5.96 (methine H), while the presence of **2b** followed from signals at δ 3.58 (br s), 3.67 (br d, J=-16.1 Hz, H_A of AB system) partially overlapped by a singlet at 3.72 (CH_3), 3.86 (br d, J= 16.1 Hz, H_B of AB system), and singlets at 12.50 and 12.95 (NH; peak ratio was 20:80 for the upfield:downfield NH signals and for the upfield:downfield CH_2 signals); aromatic protons appeared as a multiplet at δ 6.75–8.10 (14 H).

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