2,3,6-TRIAZAPHENOTHIAZINE

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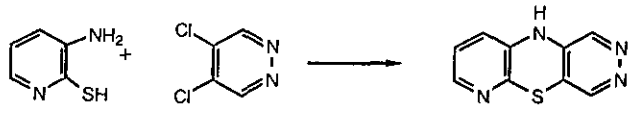
Abstract - 2,3,6-Triazaphenothiazine has been definitively synthesized and characterized. A previously reported synthesis appears to be wrong.

A compound purported to be 2,3,6-triazaphenothiazine has been described by Okafor, Castle, and Wise[1]. It was prepared by condensing 4,5-dichloropyridazine with 2-mercapto-3-aminopyridine in the presence of base:



Having need of a sample of this substance we repeated the reported work, but found in the reaction mixture no compound with the properties given. Instead, we isolated a quite different compound whose properties leave little doubt but that it is indeed the required 2,3,6-triazaphenothiazine. The properties of this compound as found by us and as recorded by Castle are:

Properties of 2,3,6-Triazaphenothiazine

	This Paper	Castle et al.
Appearance	Canary yellow	Cream-colored
mp, °C	293°(decomp.)	214-215°
Elemental Analysis	C,53.36; H,3.11; N,27.71%	C,53.24; H,3.16; N,27.38%
U.V. λ_{max},nm(ε)	∿400 (shoulder), 329 (680), 251 (3,510)	254(16,300),283(14,600)
NMR, DMSO-d6	9.16 s (1H)(broad), 8.37 s (1H), 8.15 s (1H), 7.70 m (1H), 6.80 m(2H)	9.26 s, 9.06 s

We offer the following interpretation of the data:

1. NMR Spectrum: The compound described by Castle is reported to show only two NMR signals, assigned to the protons on C(1) and C(4). One would have expected the other four protons in the molecule to generate signals, but if they did, they were not reported.

Our compound shows the proper number of signals, with the correct integrals and with the expected chemical shifts. Thus the signal at δ 9.16 is assigned to the NH because it disappears upon adding D_2O. The signals at δ 8.37 and δ 8.15 are associated with the pyridazine ring because they are unsplit and more downfield than the other ring protons. The multiplets are as would be expected for the pyridine ring protons.

2. UV Spectrum: In nitrogen heterocycles, the HOMO is the non-bonding orbital of the unshared pair on the nitrogen atom and the lowest energy transition is n → pi*. Such disallowed transitions result in weak absorption and small extinction coefficients[2]. 2,3,6-Triazaphenothiazine would be expected to show up to three such n → pi* bands, corresponding to the promotion of electrons on the pyridazine and the pyridine nitrogen atoms.

Castle reports only bands of high extinction coefficient. These cannot be assigned to the expected n → pi* transitions. We find two long wavelength, low-intensity bands, one as a shoulder at approx. 400 nm and the other with λ_{max} 329 nm.

3. Elemental Analysis: There are several ways in which the two bifunctional reactants could combine, and indeed, Castle reports the formation of bis-sulfides, contrary to their expectation, in closely related cases. It is not at all easy, however, to envision alternative structures which could reasonably be produced and which would fit the analytical data for carbon, hydrogen and

nitrogen found by ourselves and by the earlier workers. We can think of none which would fit the spectroscopic evidence reported by them, and are at a loss to suggest what their compound might have been.

EXPERIMENTAL

Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Proton nmr data were obtained on a Varian EM 360A instrument (chemical shifts, δ, ppm, internal standard TMS) and ultraviolet spectra were recorded on a Perkin Elmer 552 spectrophotometer. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

2-Mercapto-3-aminopyridine and 4,5-dichloropyridazine. 2-Chloro-3-aminopyridine (Aldrich) was converted into 2-mercapto-3-aminopyridine according to Okafor's procedure[3]. 3,4,5-Trichloropyridazine (Aldrich) was converted into 4,5-dimethoxypyridazine according to Itai and Kamiya[4] and thence into 4,5-dichloropyridazine essentially according to the procedure of Wise and Castle[5].

2,3,6-Triazaphenothiazine (1). A solution of 2-mercapto-3-amino pyridine (0.59 g) and potassium hydroxide (0.82 g of 85%) in ethanol (110 ml) was prepared under nitrogen and added slowly and with stirring under a nitrogen atmosphere to a solution of 4,5-dichloropyridazine (0.7 g) in ethanol (70 ml). The mixture was refluxed for 10 min, then kept overnight at room temperature, under nitrogen, and filtered. The filtrate was evaporated to dryness and treated with water (20 ml). A yellow solid separated (mp 290-292°C, decomp.) (250 mg). The filtrate was evaporated to dryness and extracted several times with hot methanol. The extract was concentrated to about 7 ml and diluted with an equal volume of water. Yellow needles separated (150 mg)(mp 295°C decomp.). The filtrate was evaporated and the residue was extracted with boiling chloroform. The extracts yielded a brown gum (0.3 g). The gum and the two lots of crystals were combined and chromatographed on deactivated silica in ethanol-acetone (1:1) mixture. The first and last fractions were rejected. The others were combined and evaporated giving brown-yellow crystals (510 mg), mp 285-290°C (decomp.). These were recrystallized from ethanol (Norit) to give the triazaphenothiazine (370 mg) as yellow needles, mp 293°C (decomp.).

The above (over-elaborate) work-up procedure was adopted in a search for a compound with the properties described by Okafor, Castle, and Wise. It is probable that the required compound could be isolated by simple crystallization from ethanol or aqueous ethanol.

ACKNOWLEDGEMENT

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