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Ring Transformation Reaction of 1,2,4,5-Tetrazines to 1,2,4-Triazin-5-ols and -5-thiols by Isocyanato- and Isothiocyanatotrimethylsilane

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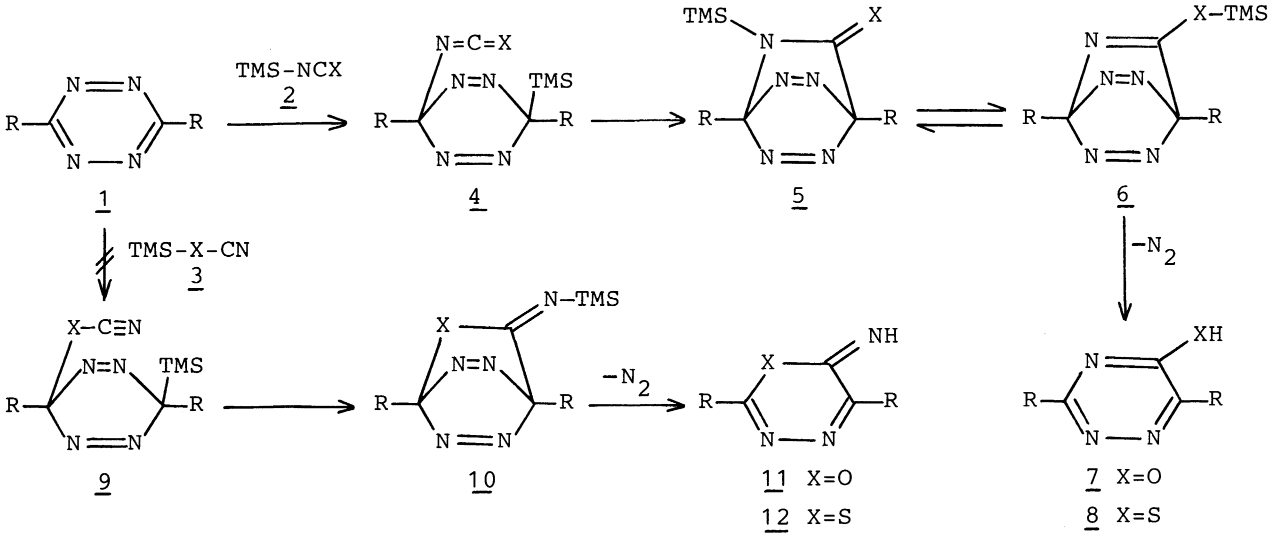
A new ring transformation reaction of 1,2,4,5-tetrazines to 1,2,4-triazin-5-ols and -5-thiols on treatment with isocyanato- and isothiocyanatotrimethylsilane, respectively, is described.

Isocyanatotrimethylsilane (TMS-NCO) and isothiocyanatotrimethylsilane (TMS-NCS) behave as electrophiles,[1] nucleophiles,[2] and dienophiles in cycloaddition reactions.[3] However, their applications to organic synthesis have been less studied than other silylated pseudo-halides such as azido-, cyano-, and halogenotrimethylsilane.[4] In the previous paper[5] intending to use organosilicon reagents for heterocyclic synthesis, we have reported a ring transformation reaction of 1,2,4,5-tetrazines (1) to 4-aminopyrazoles by use of cyanotrimethylsilane (TMS-CN). Consideration of the reaction mechanism led us to an idea that a reaction of 1[6] with TMS-NCO or TMS-NCS instead of TMS-CN would proceed through a similar reaction pathway to give 1,2,4-triazin-5-ols or -5-thiols, respectively. Now this new ring transformation reaction has been achieved and is reported in this paper.

Treatment of 1a-d (0.1 mmol) with TMS-NCO (2.0 mmol) in DMF (5-10 ml) at room temperature or at reflux under nitrogen atmosphere gave 1,2,4-triazin-5-ols



1, 7, 8 a: R=2-pyridyl, b: R=3-pyridyl, c: R=4-pyridyl, d: R=CO_2Me

(7a-d)[7] in good yields. Similar treatment of 1a, c with TMS-NCS afforded 1,2,4-triazine-5-thiones (8a, c),[7] whereas 1b, d yielded unseparable mixtures. Neither TMS-NCO nor TMS-NCS reacted with diphenyltetrazine. The structures of 7 and 8 were established especially on the basis of the similarity of the UV spectrum of 7a to that of 6-phenyl-3-(2-pyridyl)-1,2,4-triazin-5-one[8] and conversion of 7c to 8c in 78% yield on treatment with Lawesson's reagent[9] in pyridine at reflux, excluding isomeric 1,3,4-oxadiazines (11) and 1,3,4-thiadiazines (12) whose formations would be possible according to the reaction mechanisms mentioned below.

The reaction would begin with attack of isocyanate or isothiocyanate anion[2] on the C-3 position of 1, similarly to the reaction of 1 with TMS-CN,[5] to give 4, which would cyclize[10] to yield bicyclic intermediates 5 or 6. Subsequent extrusion of nitrogen from 5 or 6 would result in the formation of 7 or 8. On the other hand, attack of cyanate or thiocyanate anion, arising from an equilibrium $2 \rightleftharpoons 3$,[2] on 1 to form 11 or 12 through intermediates 9 and 10 was not observed in the present case. An alternative route to 7 and 8 through 5 obtainable on cycloaddition[3] of TMS-NCX to 1[11] was excluded because no reaction of 1 with methyl or phenyl isocyanate in DMF occurred.

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7) All compounds gave satisfactory elemental analysis. 7a: 94% yield; mp 240-243 °C; MS m/z 251 (M$^+$); IR (KBr) 3050-2800, 1642, 1575 cm^{-1}; UV (MeOH) 237 (15 800), 272 (14 600), 315 (10 200) nm. 7b: 85% yield; mp 290-295 °C; MS m/z 251 (M$^+$); IR (KBr) 2825, 1590, 1575, 1535 cm^{-1}. 7c: 87% yield; mp$>$300 °C; IR (KBr) 2800, 1605, 1590, 1570 cm^{-1}. 7d: 83% yield; mp 163-165 °C; MS m/z 213 (M$^+$); IR (KBr) 3150-2800, 1765, 1720, 1635, 1575 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 3.91 (s, 3H), 3.97 (s, 3H), 12.21 (br s, 1H). 8a: 43% yield; mp 220-270 °C (assumed to be a mixture of thiol and thione tautomers); MS m/z 267 (M$^+$); IR (KBr) 3140-2750, 1590, 1570 cm^{-1}. 8c: 49% yield (obtained as a salt of acetic acid on recrystallization from acetic acid); mp 265-300 °C; MS m/z 267 (M$^+$); IR (KBr) 2530, 1695, 1625, 1600 cm^{-1}.

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