Rearrangement of *v*-Triazolo[4,5-*d*]pyrimidines

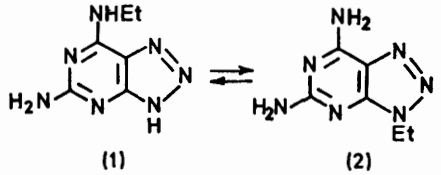
By CARROLL TEMPLE, JUN.,* BUFORD H. SMITH, JUN., and JOHN A. MONTGOMERY
(*Kettering-Meyer Laboratory, Southern Research Institute, Birmingham, Alabama* 35205)

Summary The Dimroth and *retro*-Dimroth rearrangement of a *v*-triazolo[4,5-*d*]pyrimidine system is described.

THE Dimroth rearrangement of heterocyclic compounds involves the interchange of exocyclic and endocyclic nitrogen atoms.[1] Conversion of one *v*-triazolo[4,5-*d*]pyrimidine into another is a special type of Dimroth rearrangement involving exocyclic and endocyclic C–N moieties. Previously, the rearrangement of 7-amino-3-benzyl-3*H*-*v*-triazolo[4,5-*d*]pyrimidine to the 7-benzylamino-isomer was unsuccessful.[2]

The triazolo-pyrimidine (**2**) was prepared as described by amination of the corresponding 7-chloro-compound.[3] Treatment of the known 5-amino-7-chloro-*v*-triazolo[4,5-*d*]-pyrimidine[4] with aqueous ethylamine gave the isomer of (**2**), (**1**).

Refluxing of a solution of (**2**) in dimethylacetamide (DMAC; b.p. 163—165°) for *ca.* 85 h gave unchanged (**2**) and traces of the rearrangement product (**1**) identified by t.l.c., but, in contrast, refluxing of a solution of (**1**) in DMAC for *ca.* 18 h gave mainly the rearrangement product



(**1**) (**2**)

(**2**) containing only traces of unchanged (**1**) (t.l.c.).† The rearrangement of (**1**) was also examined in pyridine (b.p. 112—115°), 2-picoline (b.p. 128°), and 2,4-lutidine (85% minimum; b.p. 155—157°) under reflux to give 65 (18 h), 76 (16 h), and 90% (16 h) conversion into (**2**), respectively, these values being determined by measurement of the integrated intensities of the $MeCH_2$ signals for (**1**) and (**2**) in the n.m.r. spectra [$(CD_3)_2SO$; Me_4Si internal reference]

† Traces of unidentified components were observed on many of the chromatograms.

of the products. In pyridine the isomer mixture was not at equilibrium since refluxing of a solution of (**1**) in this solvent for 132 h gave (**2**) containing only traces of (**1**) (t.l.c.). Also, in pyridine the rearrangement appeared to be irreversible because refluxing of a solution of (**2**) in this solvent for the same period of time (132 h) gave none of (**1**) (t.l.c.). Presumably this rearrangement involves a 5-diazopyrimidine intermediate, which favours ring closure to the amino-group of greater nucleophilicity.[5] Refluxing of a solution of (**1**) in pyridine containing an equivalent amount of β-naphthol to trap the 5-diazopyrimidine intermediate was unsuccessful; the product was a mixture of (**1**), (**2**), and β-naphthol (t.l.c.).

The rearrangement (**1**) → (**2**) depends not only on the temperature, but also on the basicity of the solvent. When a solution of (**1**) in dibutylamine (b.p. 159—161°; pK_a *ca.* 11) was heated at 130° for 16 h, no rearrangement to (**2**) was observed (t.l.c.), which suggested that the anion of (**1**) undergoes rearrangement less readily than (**1**) itself. This surmise was confirmed by refluxing a solution of the sodium salt of (**1**) in 2-picoline for 16 h to give a product that contained no (**2**) (t.l.c.).‡ Further, when separate solutions of (**1**) in pyridine (pK_a^{25} 5·17)[6] and in 2-picoline (pK_a^{25} 5·97)[6] were heated at *ca.* 110° for 18 h, the n.m.r. spectra of the products indicated 37 and 25% conversion into (**2**), respectively. Presumably, the amount of rearrangement decreases as the concentration of the anion (**1**) increases. Although this result suggested that the rearrangement of (**2**) to (**1**) might be favoured by a strong base, no rearrangement was observed when a solution of (**2**) was refluxed in dibutylamine for 18 h[7] Apparently, however, the system of (**1**) and (**2**) in DMAC described above is at equilibrium. Refluxing of a solution of (**2**) in DMAC containing potassium carbonate for 18 h shifted the equilibrium so that only (**1**) (potassium salt) was observed (t.l.c.). This result was confirmed by the u.v. spectrum of the crude rearrangement product.

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‡ The product of this reaction gave analytical data consistent with its formulation as the hemihydrate as the sodium salt of (**1**).

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[6] H. C. Brown and X. R. Mihm, *J. Amer. Chem. Soc.*, 1955, **77**, 1723.
[7] Similarly 1-alkyl-5-amino-1,2,3-triazoles resist Dimroth rearrangement. See ref. 1.