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UNUSUAL DIMROTH REARRANGEMENT OF AN ALLYL-1,2,4-TRIAZOLO[4,3-c]PYRIMIDINE

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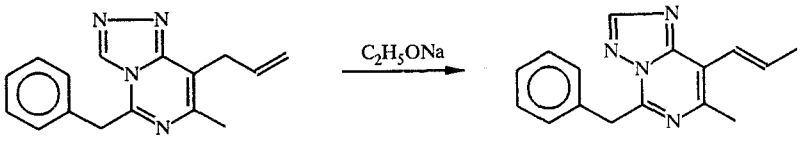
Refluxing 4-allyl-7-benzyl-5-methyl-1,2,4-triazolo[4,3-c]pyrimidine in an alcohol solution of sodium ethylate causes a Dimroth rearrangement together with a prototropic isomerization of the allyl fragment to give 7-benzyl-5-methyl-4-propenyl-1,2,4-triazolo[2,3-c]pyrimidine.

A previous report [1] concerned the conversion of 7-benzyl-5-methyl-1,2,4-triazolo[4,3-c]pyrimidine to the isomeric 7-benzyl-5-methyl-1,2,4-triazolo[2,3-c]pyrimidine via a Dimroth rearrangement. In particular, it was found that the recyclization process could be monitored directly in an NMR tube.

To continue investigation of the rearrangement we have studied the reaction of the analogous allyl derivative, i.e., 4-allyl-7-benzyl-5-methyl-1,2,4-triazolo[4,3-c]pyrimidine.

A series of examples of the Dimroth rearrangement of allyl containing systems has been reported [2, 3]. It was found that an allyl substituent at position 1 of the pyrimidine caused a significant (several times) increase in the rearrangement reaction rate, whereas an allyl group in position 5 caused no significant change.

In the example discussed the recyclization product was obtained in 82% yield by refluxing a solution of the starting triazolopyrimidine in an ethanol solution of sodium ethylate for 1 h. Breakdown of the product was not observed. Comparison of the PMR spectra of the starting and isomeric products showed that both a Dimroth rearrangement and prototopic isomerization of the allyl to a propenyl substituent had occurred. The PMR spectrum of the starting triazolopyrimidine showed signals characteristic of an $ABMX_2$ spin system together with a triazole ring proton signal at 8.67 ppm. By contrast, the isomeric product showed signals for an ABX_3 system with an E-configured double bond and a triazole ring proton signal at higher field (8.37 ppm). In the PMR spectra of these molecules it was also found that the phenyl ring signal for the starting material appears as a sharp singlet whereas the isomerized product shows a multiplet of width about 0.3 ppm. This is apparently connected with some hindrance to rotation of the benzyl group.



I II

The isomers also differed significantly in their chromatographic mobility and mass spectral fragmentation. The molecular ions of both isomers were quite stable, probably because each undergoes cyclization of the side chain olefinic carbon onto the adjacent nitrogen atom of the annelated triazole ring. This is a characteristic of allyl- or alkenylazines which also contain groups next to an sp^2 hybridized nitrogen atom. A tricyclic ion radical is formed. In the case of I this is stabilized as ion mass 263 by elimination of a hydrogen atom whereas II prefers to lose a methyl group to form the highly stabilized 249 ion. Thus, mass spectral analysis of both compounds allowed us to assign the position of the double bond with confidence.

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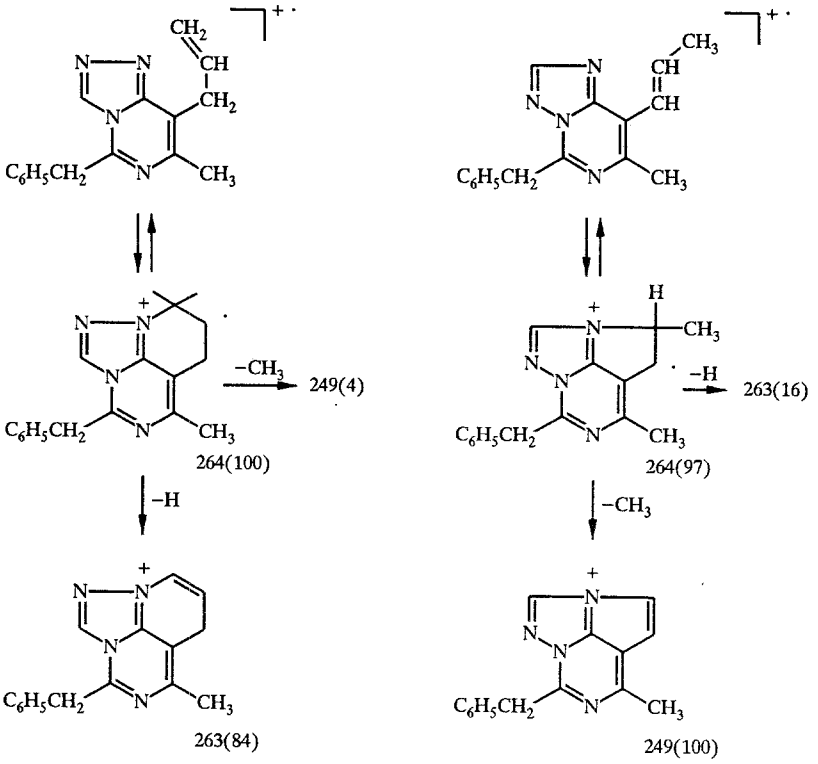

It should be noted that previous literature reports of the Dimroth rearrangement of systems containing an allyl group have not described prototropic allylic rearrangement. Thus, the reaction described in this report is a novel one.

EXPERIMENTAL

PMR Spectra were recorded on a Varian T-60 instrument using TMS standard. Mass spectra were recorded on an MK-1321 spectrometer with direct sample introduction into the ion source and an ionization energy of 70 eV. The reaction progress and product purities were monitored using Silufol UV-254 TLC plates with benzene–acetone (3:1) developing solvent and iodine vapor visualization.

Elemental analytical data for C, H, and N agreed with that calculated.

4-Allyl-7-benzyl-5-methyl-1,2,4-triazolo[4,3-c]pyrimidine (I). A mixture of 5-allyl-2-benzyl-4-hydrazino-6-methylpyrimidine (2.54 g, 0.01 mole) and ethyl-o-formate (8 ml) was refluxed for 6 h. After distillation of excess ester and ethanol the mixture was cooled and the residue recrystallized from hexane to give product (1.96 g, 74%) with mp 121-122°C and R_f 0.65. PMR Spectrum ($CDCl_3$): 2.54 (3H, s, 5-CH_3), 3.77 (2H, dt, $\underline{CH_2}CH{=}CH_2$, J = 6.1, J_2 = 1.1 Hz), 4.44 (2H, s, $CH_2C_6H_5$), 5.10 and 5.25 (2H, m, $=CH_2$), 6.00 (1H, ddt, =CH, J_1 = 16.5, J_2 = 10.0, J_3 = 6.1 Hz), 7.32 (5H, s, C_6H_5), 8.67 ppm (1H, s, 1-H). Mass spectrum, m/z ($I_{rel.}$, %): 264 (100), 263 (84), 249 (4), 237 (25), 236 (40), 222 (10), 187 (11), 146 (20), 91 (44).

7-Benzyl-5-methyl-4-propenyl-1,2,4-triazolo[2,3-c]pyrimidine (II). An alcohol solution of I (1.32 g, 0.005 mole) was added to an ethanol solution of sodium ethylate (0.05 g sodium in 10 ml ethanol) and refluxed for 1 h. The product was neutralized using an ethereal solution of hydrogen chloride, evaporated to dryness, hexane added to the residue, and the crystals filtered off. Recrystallization from a mixture of benzene–hexane gave II (1.08 g, 82%) with mp 97-98°C and R_f 0.8. PMR Spectrum ($CDCl_3$): 1.94 (3H, d, $=C-CH_3$, J = 6.7 Hz), 2.55 (3H, s, CH_3), 4.57 (2H, s, $CH_2C_6H_5$), 6.58 (1H, m, $\underline{CH}{=}CH{-}CH_3$, J = 18.0 Hz): 7.2-7.6 (6H, m, C_6H_5 and $CH{=}\underline{CH}{-}CH_3$), 8.37 ppm (1H, s, 2-H). Mass spectrum, m/z ($I_{rel.}$, %): 264 (97), 263 (16), 249 (100), 236 (9), 222 (5), 146 (58), 132 (13), 104 (5), 91 (22), 77 (11).

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