Tetrahedron Letters No. 31, pp 2645 - 2648, 1974. Pergamon Press. Printed in Great Britain.

STUDIES IN CLAISEN REARRANGEMENT
A NOVEL DEPROPARGYLATIVE CYCLISATION OF N-PROPARGYL-2-(PROPARGYLTHIO)-BENZIMIDAZOLE

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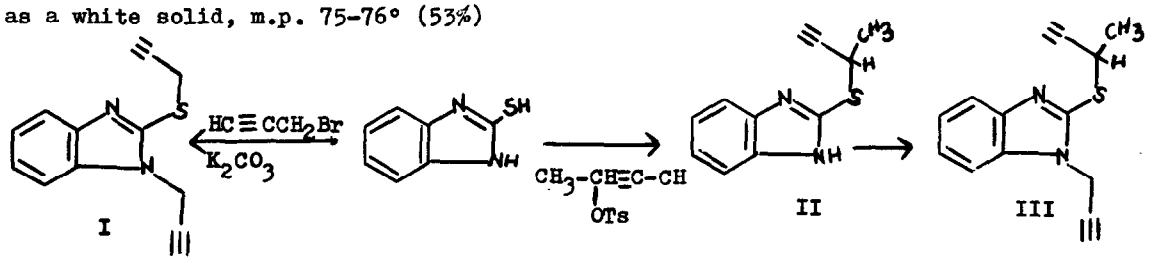
(Received in UK 30 May 1974; accepted for publication 19 June 1974)

In recent years there has been a lot of interest in the study of simple, multiple and sequential sigmatropic rearrangements involving acetylenic systems[1,2]. In continuation of our work in this area, we undertook a study of the rearrangement of N-propargyl-2-(propargylthio)-benzimidazoles, as they could undergo several interesting transformations, described below:

It could lead to a 3,3-sigmatropic rearrangement involving the propargyl thioimidate moiety[2] and a hitherto unreported type of amino propargyl Claisen rearrangement in which the nitrogen of the propargylamino group is part of a condensed heterocylic system. A second possibility is a diaza Cope rearrangement involving an N to N migration of the propargyl group, followed by a propargyl thioimidate rearrangement. So far no such Cope rearrangement seems to have been reported in literature, though a few examples of diaza Cope rearrangement in acyclic systems have recently been described[3,4]. Yet another interesting possibility is the synchronous migration of the S-propargyl to N and N-propargyl to S, involving a ten membered transition state, similar to that of the rearrangement of diaryloxy isobutylenes[5]. One more objective was to find out whether the above study would lead to simple methods of synthesis of annelated tricyclic and tetracyclic heterocycles.

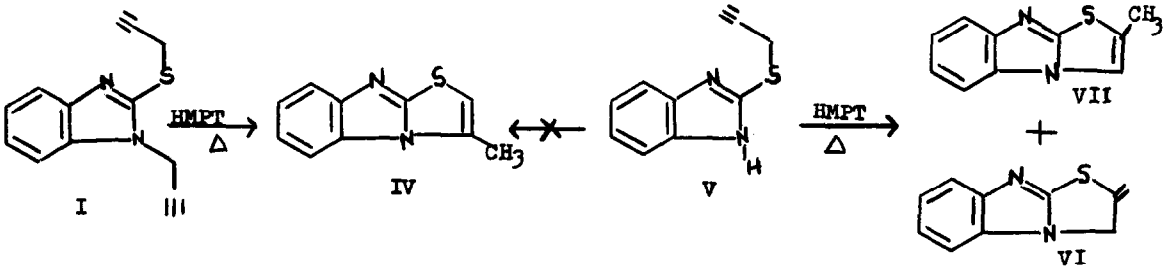
Refluxing a solution of 2-mercaptobenzimidazole with excess of

propargyl bromide in acetone in the presence of potassium carbonate for 20 hours furnished the N-propargyl-2-(propargylthio)benzimidazole I as a white solid, m.p. 75-76° (53%)



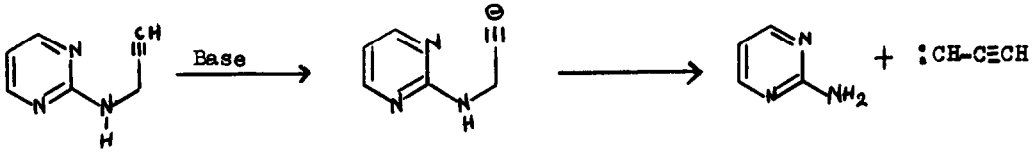
N-propargyl-2-(3-butyn-2ylthio)benzimidazole III was prepared by refluxing the butynylthiobenzimidazole II with propargyl bromide in acetone in the presence of potassium carbonate.

When a solution of the bispropargyl benzimidazole I in hexamethylphosphoric triamide (HMPT) was refluxed for 30 minutes in a nitrogen atmosphere, a tarry solid was obtained (60%), which upon column chromatography over basic alumina furnished a white solid, (30%) m.p. 163-4°. Analytical and spectral data indicated its structure to be 3-methylthiazolo(2,3-b)benzimidazole, IV. This was confirmed by comparing it with an authentic sample prepared according to the published procedure[6].



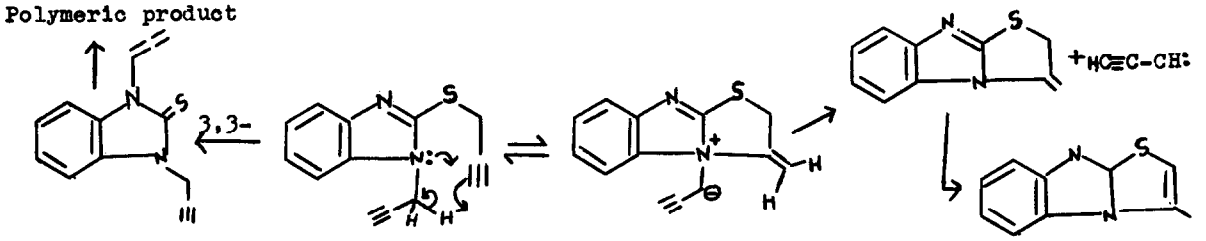
This depropargylative cyclisation was investigated in greater detail due to the following reasons: To our knowledge there seems to be no examples in literature of depropargylation of N-propargyl derivatives

in refluxing HMPT, though deallylation of N,N-diallyl anilines under pyrolytic conditions (~280°C) are known[7]. Iwai et al had observed that 2-(2-propynyl amino) pyrimidine was cleaved to 2-aminopyrimidine when treated with sodium methoxide[8]. A similar depropargylation in the presence of amine bases had also been reported by Wolf and Ramin in the case of N-propargyl anilines[9]. The mechanism proposed by Iwai et al is shown below:



In our case, the fact that authentic 2-(propargylthio) benzimidazole, V under identical conditions did not lead to the 3-methylthiazolo benzimidazole IV but gave rise to a mixture of 2-methylthiazolobenzimidazole VII and the exomethylene isomer VI clearly ruled out the mechanism similar to that of Iwai et al or any other mechanism involving the intermediacy of 2-propargylthio benzimidazole V[2]. In the light of our above findings and in view of the fact that there are two different propargyl groups either of which could have been lost, we investigated this reaction in greater detail and our observations are summarised below:

When the bispropargylbenzimidazole I was heated in toluene or decalin or in a sealed tube in benzene at 160°, only extensive polymerisation was noticed though a spot corresponding to that of 3-methylthiazolo-benzimidazole could be seen in tlc. There was very little reaction when the bispropargylbenzimidazole I was refluxed in triethylamine, as seen from tlc. Similarly heating a solution of 2-methyl-N-propargylbenzimidazole VIII or 2-(methylthio)-N-propargylbenzimidazole IX in HMPT in a nitrogen atmosphere did not lead to the respective depropargylated amine. Neither 3-methylthiazolo (2,3-b)benzimidazole IV nor 2-ethylthiazolo(2,3-b)benzimidazole X, could be detected when the substituted propargyl sulphide was refluxed in HMPT for 45 minutes. On the basis of these findings, we are postulating the following mechanism;



The failure of N-propargyl-2-(3-butyn-2yl-thio)benzimidazole II to exhibit the above depropargylation may be due to the diminished electrophilic reactivity of its triple bond and a greater propensity to undergo an irreversible competitive 3,3-sigmatropic rearrangement, as alkyl substitutents on the α carbon atom of the propargyl moiety are known to accelerate such 3,3-sigmatropic rearrangements[10]. We are currently investigating the behaviour of the N-benzyl and N-phenacyl derivatives and other related compounds.

ACKNOWLEDGEMENT: We are thankful to Dr. T.R. Govindachari, Director, Ciba Research Centre, Bombay, for microanalytical and nmr spectra. We are grateful to the Indian National Science Academy for supporting this research project.

1. K.K. Balasubramanian and B. Venugopalan, Tetrahedron Letters, 2907 (1973) and references cited therein.
2. K.K. Balasubramanian and B. Venugopalan, Tetrahedron Letters, (in press) (1974).
3. Fritz Volgtle and Ernst Goldschmitt, Angew.Chem., (Int.edition) 767 (1973).
4. R.V. Stevens and Edward E. McEntire.Chemical Communications, 18, 662 (1973).
5. Review article on 'Trimethylenemethane and related disubstituted isobutenes' by Francis Weiss, Quarterly reviews, Vol.XXIV No.2.(1970).
6. Issei Iwai and Tetsuo Hiraoka, Chem. and Pharm.Bulletin(Japan)12 (7) 813 1964.
7. S. Marcin Kie Wicz, Bull.Acad.Pub.Sci.Ser.Sci.Chim. 19, (10) 609-13 (1971); CA. 33611 x (1972).
8. Issei Iwai and Tetsuo Hiraoka, Chem.And Pharm.Bulletin 12 (7) 812 (1964).
9. V. Wolf and D. Ramin, Ann. 633 30 (1960).
10. Morton Harfenist and Edna Thom, J.Org.Chem. 6, 841 (1972).