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SYNTHESIS AND THERMAL BEHAVIOUR OF A NOVEL DIAZAENEDIYNE AND ITS COPPER(II)-COMPLEX

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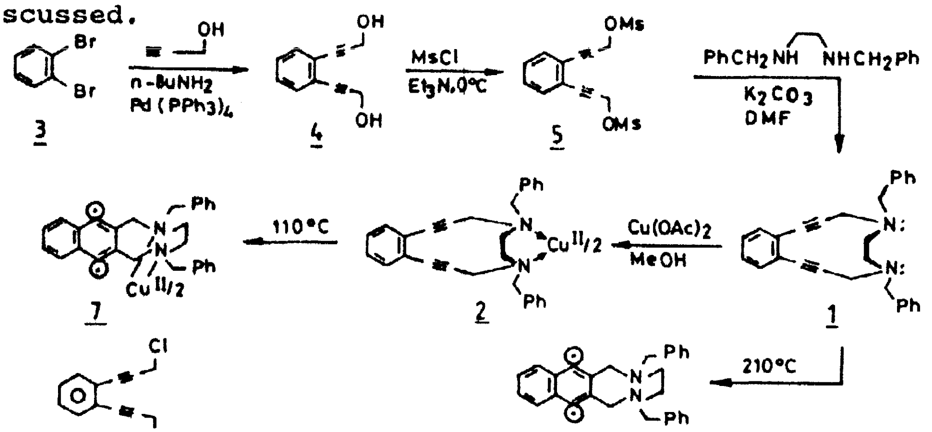
Abstract **: A novel 12-membered diazaenediyne and its Cu(II)-complex have been synthesized. Differential Scanning Calorimetric (DSC) measurements revealed a depression of onset temperature for Bergman cyclization.**

Bergman cyclization (BC)[1] which is the key process for the cytotoxic activity of enediynes[2] has been a subject of considerable interest in recent years. The rate of BC is influenced by ring-size[3], state of hybridization[4] incorporation of heteroatom[5] or strained ring system[6] and metal-ion complexation[7]. Recently[8] we have synthesized a 10-membered azaenediyne and showed its spontaneous cycloaromatization ($t_{1/2} \approx 36$h at 30°C). Herein we report the synthesis of a novel diazaenediyne 1 and its copper (II) complex 2. Their thermal behaviour is also discussed.



Scheme 1

1,2-Dibromobenzene was first converted into the diol 4 by a double Pd(o)-catalysed coupling[9]. Treatment of 4 with methanesulphonyl chloride (2 eq) and triethylamine (2 eq) at 0°C for 15 min gave the dimesylate 5. Longer reaction time produced substantial amount of the dichloride 5a.

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The dimesylate 5 was then converted into the target diazaenediyne 1 by double N-alkylation with N,N'-dibenzylethylenediamine in the presence of K_2CO_3 in DMF. Compound 1 crystallized from hexane-ethylacetate in needles, m.p. 123°C. The ^1H NMR spectrum showed three sharp singlets (each 4H) at δ 3.05, 3.56 and 3.69 apart from the aromatic signals at δ 7.24-7.43. Further confirmation about the structure was obtained from the mass spectrum which showed the M^+ peak at m/z 390. DSC measurements[10] showed the onset temperature for BC to be ~210°C. Since various metal complexes are known for their DNA-cleaving activity[11], attempts were made to prepare Cu(II)-complexes of enediyne 1. Thus, when a methanolic solution of 1 and $Cu(OAc)_2$ (2:1 mmolar ratio) was refluxed (10h) and solvent removed. brown Cu(II)-complex was obtained. Its ^1H-NMR spectrum ($CDCl_3$) showed the aromatic signals at δ 8.3-6.9 while all the pairs of methylene protons appeared as a very broad signal in the range δ 4.0-3.0. DSC measurement of the complex 2 showed the onset temperature for BC to be 110°C indicating a dramatic reduction of activation energy for BC upon complexation. This could be due to the formation of a smaller 11-membered metallocycle in the complex compared to the 12-membered ring present in 1. DTMM calculation also showed a considerable shortening of distance between the reacting acetylenes upon complexation.

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Reference

1. Jones, B. R.; Bergman, R. G. *J. Am. Chem. Soc.* 1972, 94, 660; Bergman, R. G. *Acc. Chem. Res.* 1973, 6, 25; Lockhart, T. P.; Comita, P. B.; Bergman, R. G. *J. Am. Chem. Soc.* 1981, 103, 4091.
2. Nicolaou, K. C.; Dai, W. M. *Angew. Chem. Int. Ed. Engl.* 1991, 30, 1387; Grissom, J. W.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron*, 1996, 52, 6453.
3. Nicolaou, K. C.; Zuccarello, G.; Ogawa, Y.; Schweiger, E. J.; Kumazawa, T. *J. Am. Chem. Soc.* 1988, 110, 4866.
4. De Voss, J. J.; Hangeland, J. J.; Townsend, C. A. *J. Am. Chem. Soc.* 1990, 112, 4554.
5. Sakai, Y.; Nishiwaki, E.; Shishido, K.; Shibuya, M. *Tetrahedron Lett.* 1991, 32, 4363.
6. Nicolaou, K. C.; Sorenson, E. J.; Discordia, R.; Hwang, C. K.; Minto, R. E.; Bharucha, K. N.; Bergman, R. G. *Angew. Chem. Int. Ed. Engl.* 1992, 31, 1044; Basak, A.; Khamrai, U. K. *J. Chem. Soc. Chem. Commun.* 1995, 749; Banfi, L.; Guanti, G. *Angew. Chem. Int. Ed. Int. Engl.* 1995, 34, 2393.
7. Konig, B.; Hollnagel, H.; Ahrens, B.; Jones, P. G. *Angew. Chem. Int. Ed. Engl.* 1995, 34, 2538.
8. Shain, J. C.; Khamrai, U. K.; Basak, A. *Tetrahedron Lett.* 1997, 38, 000.
9. Just, G.; Singh, R. *Tetrahedron Lett.* 1987, 28, 5981.
10. Burkhead, K.; Rutters, H. *Tetrahedron Lett.* 1994, 35, 3501.
11. Sigman, D. S. *Acc. Chem. Res.* 1986, 19, 180; Ranganathan, D.; Mishra, R. K.; Patel, B. K.; Vaish, N. K. *Proc. Ind. Acad. Sci.* 1994, 106, 1071.