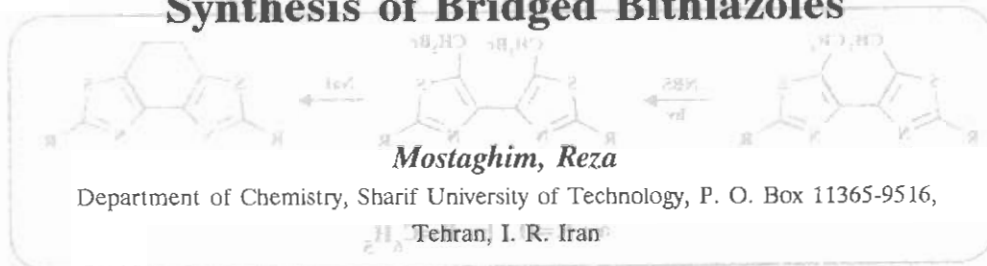


Synthesis of Bridged Bithiazoles



ABSTRACT: Bridged bithiazoles (5,5'-ethylene-4,4'-bithiazoles) are synthesized as a good chelating agent.

KEYWORDS: Bithiazoles, Bridged bithiazoles, Chelating agent

Bleomycines are a family of compounds that have potent anti tumor properties. Bleomycin intercalates into the DNA helix by a bithiazole component [1-3]. Rhodium (III) complex with bithiazoles has been reported to be used in the photoproduction of hydrogen from water [4]. Bithiazoles of 2,2',-2,4',-4,5', and 5,5' connections with different substitutions such as alkyl groups have been reported [5-7,10,11]. These compounds have limited use in the selective formation of N,N'-metal complexes due to free rotation along the thiazole rings. Synthesis of bridged 5,5'-ethylene-4,4'- bithiazoles (III_a and III_b), as a good chelating agents are reported here.

The modified Hantzsch procedure for synthesis of bithiazoles (I_a and I_b) was used. These compounds were brominated at the methyl groups using NBS and light to produce II_a and II_b. Compounds II_a and II_b were then treated with NaI according to Wurtz procedure to give III_a and III_b (Scheme 1).

5,5'-Dibromomethyl-4,4'-bithiazole (II_a) and 5,5'-Dibromomethyl-2,2'-diphenyl-4,4'-bithiazole (II_b)

To a solution of a 1.0 mmole of I_a (or I_b) [5], 1.0 mmole benzoyl peroxide (0.214 g) in 200 mL of carbon disulfide and 2.0 mmoles (0.356 g) of NBS was added. The mixture was refluxed and photolyzed with

a UV lamp (273 nm) for 1.5 hours. The reaction mixture was then filtered and the solvent was removed to yield some solid product(s). Recrystallization from low boiling point petroleum ether, afforded II_a (or II_b).

II_a: (45 mg, 0.127 mmol) yield 22.9%, m.p. 201°C, IR(KBr): 3076(C-H), 1501(C=C), 1340(C=N) cm⁻¹, ¹H NMR: 8.7(s, 2H), 5.3(s, 4H).

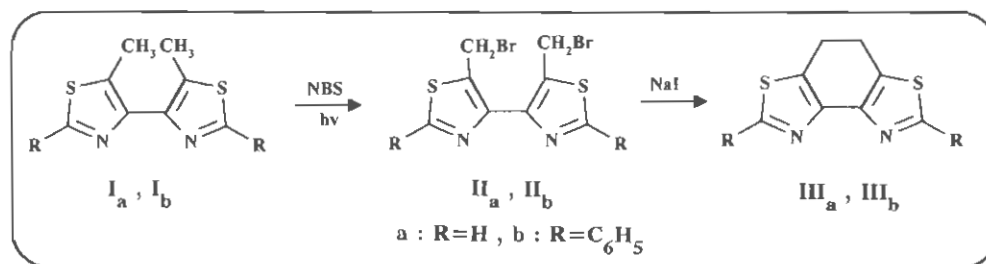
II_b: (120 mg, 0.23 mmol) yield 34.4%, m.p. 236°C, IR(KBr): 1570(C=C), 1910(C=N) cm⁻¹, ¹H NMR: 5.7(s, 4H), 8.5-7.9(m, 10H).

5,5'-Ethylene-4,4'-bithiazole (III_a) and 5,5'-ethylene-2,2'-diphenyl-4,4'-bithiazole (III_b)

A mixture of 1.0 mmoles of II_a (or II_b) and 3.0 mmoles (0.450 g) sodium iodide in 20 mL absolute ethanol was stirred at room temperature for 20 minutes to afford the solid product(s). The mixture was then filtered and the product(s) was collected.

III_a: m.p. 167°C, Anal. Calcd; C: 49.48%, H: 3.09, N: 14.43%, S: 32.7%, found C: 49.40%, H: 3.1%, N: 14.3%, S: 32.8%. IR(KBr): 3046(C-H), 1434(C=C), 1387(C=N) cm⁻¹, ¹H NMR: 8.6(s, 2H), 5.6(s, 4H); Mass: (m/e), 194(M⁺, 100%), 195(10%), 196(8%), 83(70%).

III_b: Anal. Calcd; C: 69.36%, H: 4.62%, N: 8.09%, S:



Scheme 1

18.49%, Found: C: 69.2%, H: 4.0%, N: 8.1%, 18.5%. IR(KBr): 1510(C=C), 1418(C=N), 1316(C=N) cm^{-1} , ^1H NMR: 5.67(s, 4H), 7.1-8.5(m, 10H). Mass: 346 (M^+ , 16%), 347(8%), 348(10.5%), 160(100%).

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REFERENCES

- [1] Hay, J., Shahzeidi, S. and Laurent, G., *Archives of Toxicology*, **65**, 81(1991).
- [2] Craciuneacu, D. G., Fulani, A., Scarcia, V. and Dardio, A., "Biological Trace Element Research", Vol. 8, Humana press inc. Italy, pp. 251-261 (1985).
- [3] Tang, H., Wang, T. L. H., Gu, W. and Gu, C., *Fundam. Res. Organomet. Chem.*, 1327(1980).
- [4] Stoessel, S. J. and Stille, J., *Macromolecules*, **25**, 1832(1992).
- [5] Erlenmeyer, H. and Ueberwasser, H., *Helv. Chim. Acta.*, **23**, 1268(1940).
- [6] Beatrice, P. and Pietro, T., *J. Het. Chem.*, **27**, 463(1990).
- [7] Mostaghim, R., "Doct. Ing. Thesis", University of Marseill France (1981).
- [8] Roussel, P. and Metzger, J., *Bull. Soc. Chem. Franc.*, 2075(1962).
- [9] Dyson, G. M., Hunter, R. F., Jones, G. W. and Styles, J., *Indian, J. Chem.*, 147(1931).
- [10] Sarkar, B. R. and Lahiri, S. C., *Indian, J. Chem.*, 151(1984).
- [11] Baker, A. T. and Goodwin, H. A., *Aust. J. Chem.*, **38**, 851(1985).