Third International Electronic Conference on Synthetic Organic Chemistry (ECSOC-3), www.mdpi.org/ecsoc-3.htm, September 1-30, 1999

[A0030]

Novel Imidazole Analogues of Stilbene: Synthesis and Characterization of *Cis*- and *Trans*-1,2-bis(4-nitro-1-*p*-methoxybenzylimidazol-5-yl)ethene

Saika Siddiqui and Ramachandra, S. Hosmane*

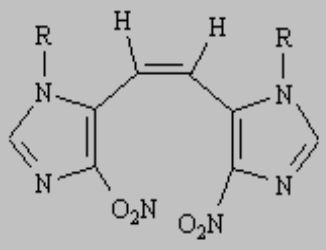
Laboratory for Drug Design and Synthesis, Department of Chemistry & Biochemistry
University of Maryland, Baltimore County (UMBC), 1000 Hilltop Circle
Baltimore, Maryland 21250, USA
E-mail: hosmane@umbc.edu

Received: 17 August 1999 / Uploaded: 21 August 1999

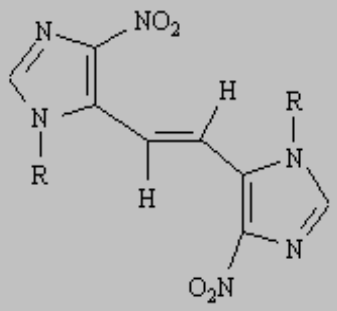
Keywords: Synthesis, Imidazole Analogues of Stilbene, Versatile Synthetic Intermediates.

INTRODUCTION

Stilbenes are an important class of organic compounds carrying a wide variety of useful applications in organic synthesis. These applications include, but are not limited to, asymmetric dihydroxylation, photocyclization, photodimerization, and synthesis of diphenyl acetylenes, bromohydrins, and benzils. Heterocyclic analogues of stilbenes are of interest not only for exploring these various applications but also for their inherent potential to serve as key precursors to the synthesis of a host of novel as well as known heterocycles containing fused imidazole ring systems. We present here the synthesis and characterization of the title *cis*- and *trans*-1,2-bis(4-nitro-1-*p*-methoxybenzylimidazol-5-yl)ethene, **I** and **II**.



I



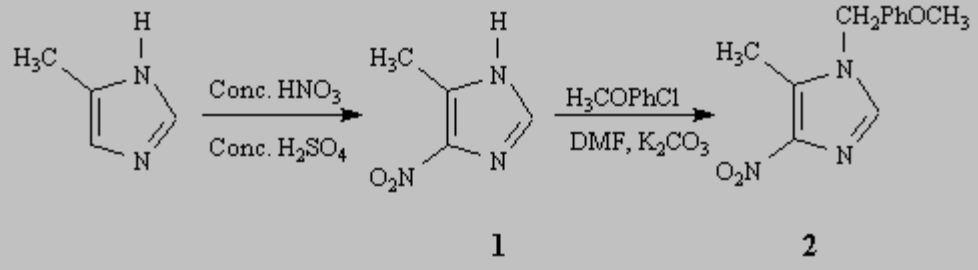
II

RESULTS & DISCUSSION

The synthesis of title compounds **I** and **II** started with 4-methylimidazole, which was nitrated[1] using a mixture of concentrated sulfuric and nitric acids to obtain 5-methyl-4-nitro-1*H*-imidazole (**1**) (**Scheme 1**). The crude nitrated product was treated with *para*-methoxybenzyl chloride and potassium carbonate in DMF to yield crystals of 4-nitro-1-*p*-methoxybenzyl-5-methyl-1*H*- imidazole (**2**) as a single regioisomer, as determined from NMR data. The regioisomeric assignment of **2** was based upon (a) comparison of the benzyl absorptions of **2** in its ^{1}H NMR spectrum

with those of several other benzyl-substituted nitroimidazoles previously synthesized in this laboratory, and (b) the established fact that the alkylation of nitroimidazoles predominantly yield substitutions at the nitrogen atom farther away from the nitro group.[3]

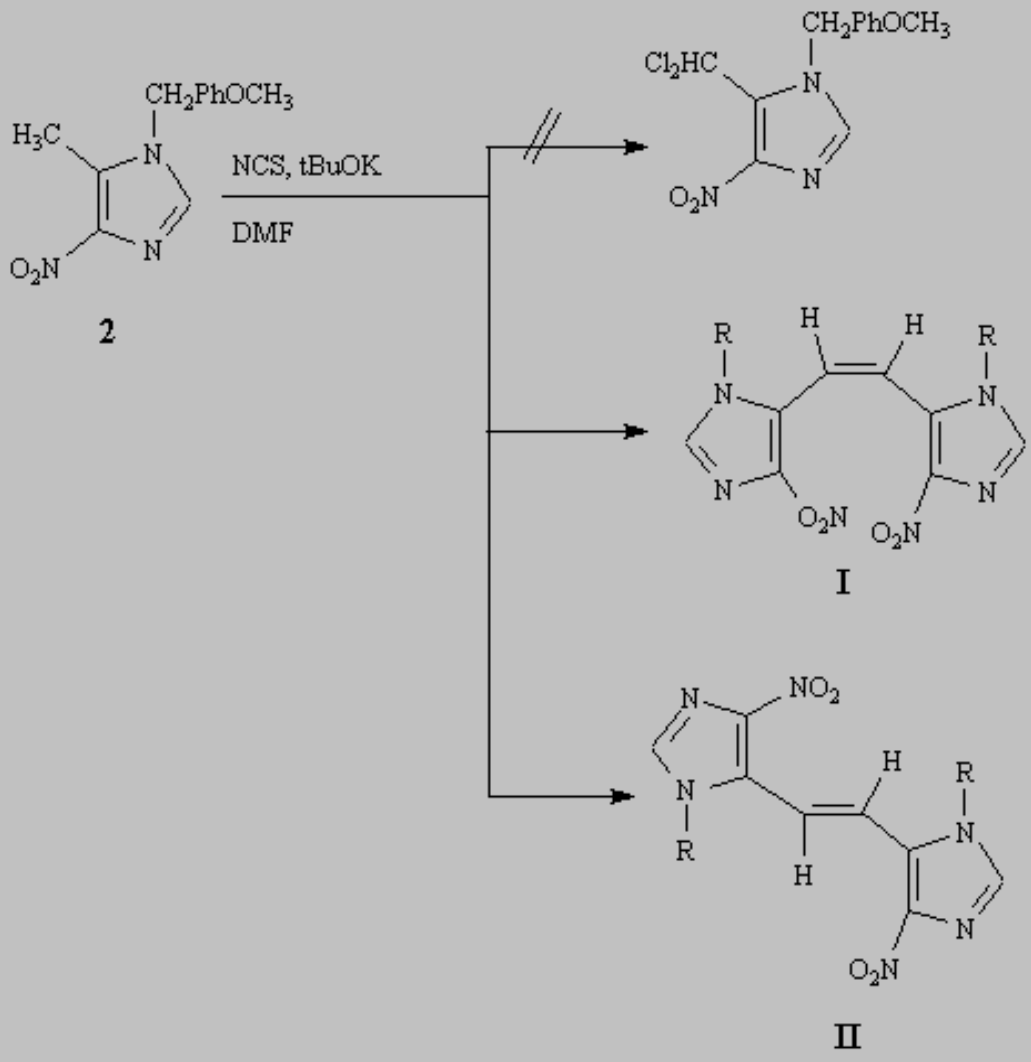
SCHEME 1



1 **2**

The target dimers **I** and **II** were prepared (**Scheme 2**) by the reaction of **2** with *N*-chlorosuccinimide (NCS)[4] in the presence of potassium *tert*-butoxide in DMF. The same result was obtained with *N*-bromosuccinimide (NBS). The ratio of *cis* (**I**) and *trans* (**II**) isomers in the

SCHEME 2



2 **I** **II**

product mixture depended upon the mode of addition of the reactants. Thus, when a solution of NCS in DMF was

added to the mixture of **2** and potassium *tert*-butoxide in DMF, both **I** and **II** formed, and the yield was poor, perhaps due to the formation of polymers in addition to the dimers. On the other hand, the *trans* isomer **II** was the major product upon slow, reverse addition of **2** and potassium *tert*-butoxide to a solution of NCS in DMF. The ^{1}H NMR of the product mixture obtained by direct addition of NCS (the first method described above) exhibited two sets of peaks, while that obtained by the reverse addition showed only a single set of peaks.

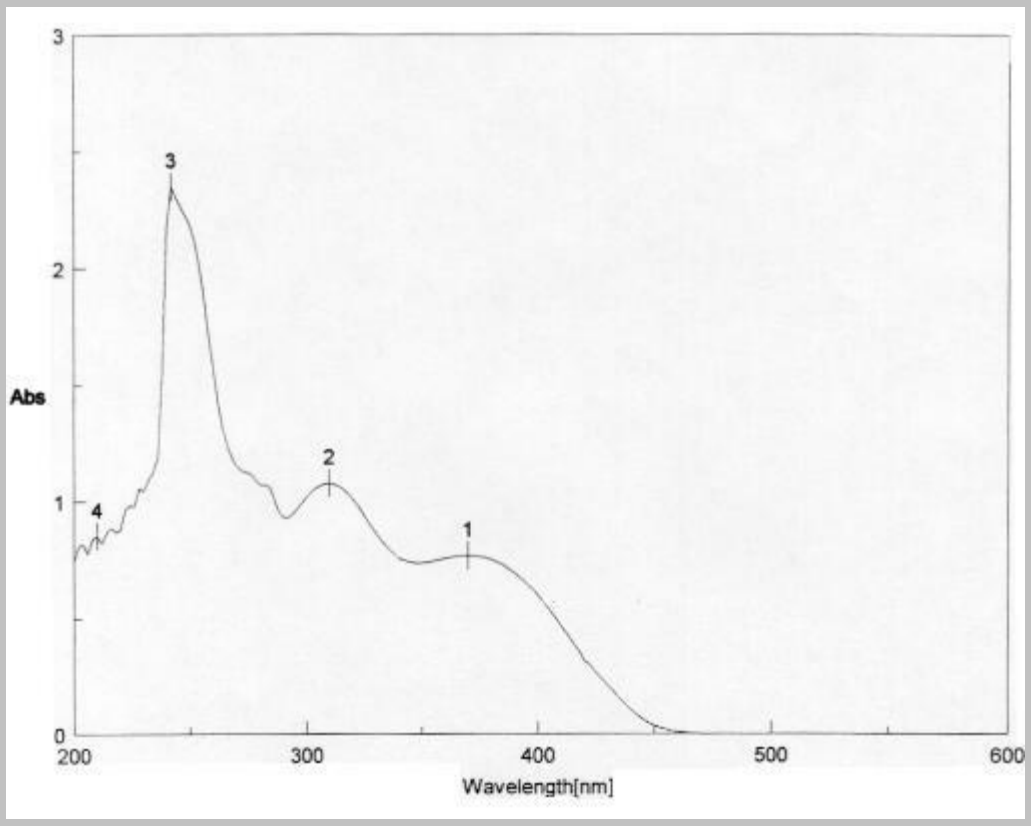


Figure 1: The UV absorbance spectrum of the mixture of **I** and **II** in chloroform: $_{max}$: 1: 370; 2: 310; 3: 242; 4: 210 nm

The structural distinction between the two geometric isomers was achieved by comparing the UV absorbance data of the mixture **I** and **II** with that of **II** alone. The UV absorbance spectra of **I** and **II**, depicted in **Figure 1** showed two peaks above 300 nm, one at $_{max}$ 310 nm and 370 nm. The UV absorbance spectra of **II** in **Figure 2**, on the other hand, showed only one peak at $_{max}$ 370 nm. The *cis* isomer **I**, with its two-charged nitro groups in close proximity, is expected to absorb at a lower wave number (higher energy) than the *trans* isomer **II**. Thus **I** and **II** were assigned the *cis* and *trans* configurations, respectively. The mass spectrometric and microanalytical data were also consistent with the dimeric structures of **I** and **II**.

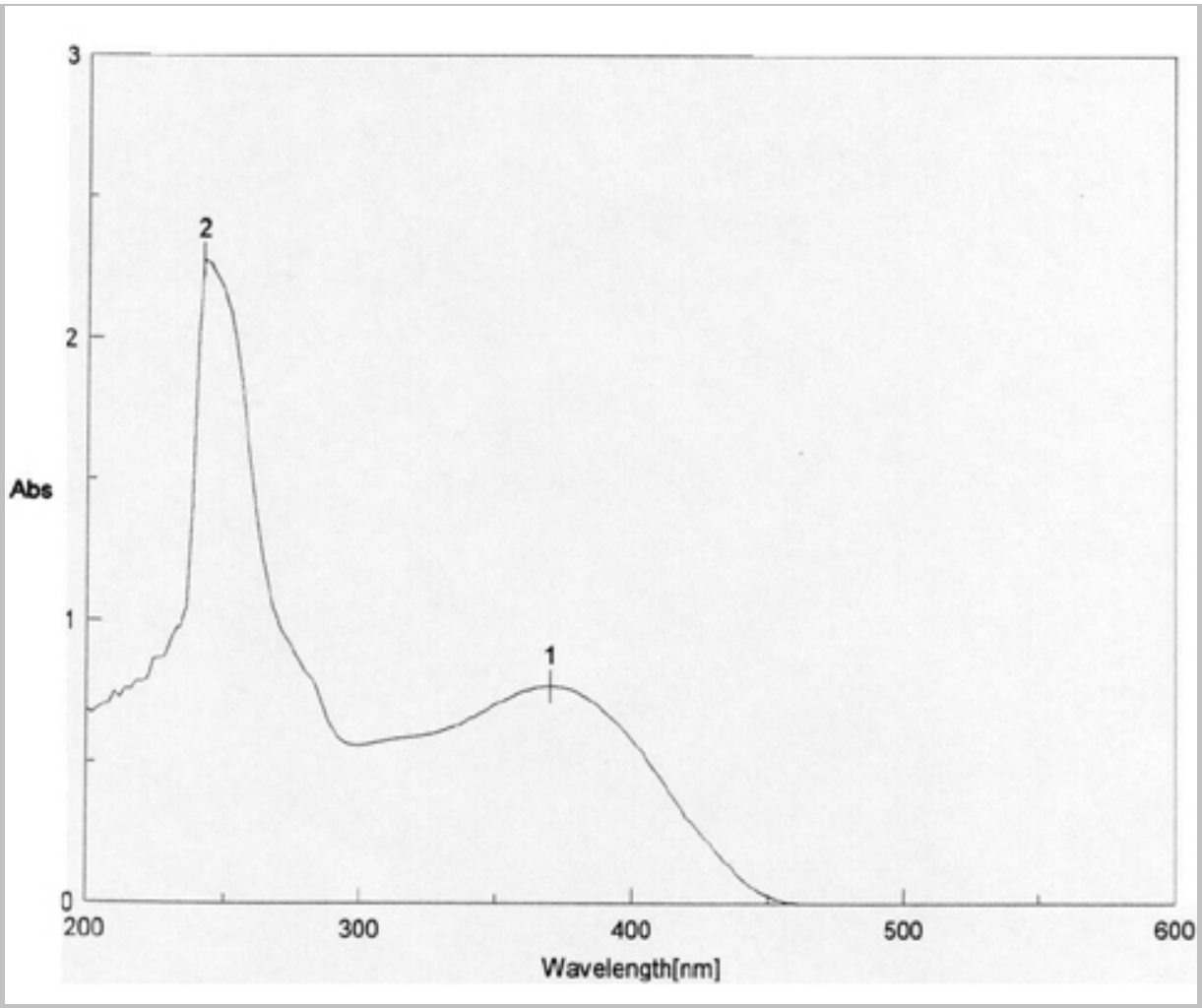
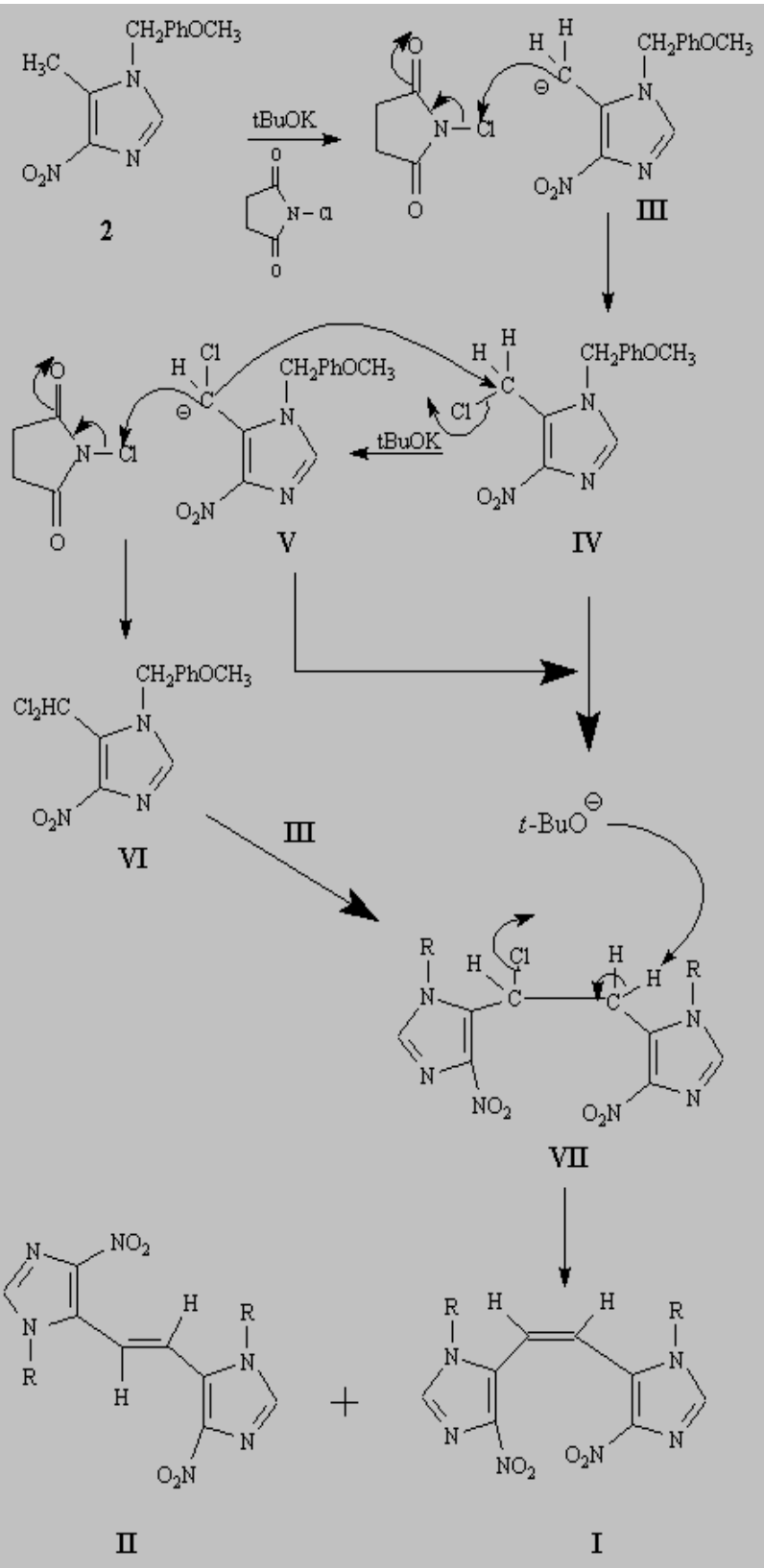


Figure 2: UV absorbance spectrum of **II** in chloroform. $_{max}$: 1: 370; 2: 242 nm.

A tentative reaction pathway for the formation of **I** and **II** from **2** is outlined in **Scheme 3**. It appears that the key intermediate is the monochloro dimer **VII**, which might be formed via a couple different routes, including the nucleophilic displacement reaction of the carbanion **V** on the initially formed monochloro species **IV** or by the attack of carbanion **III** on the dichloro species **VI**. The intermediate **VII** undergoes further dehydrohalogenation in the presence of potassium *t*-butoxide to yield the observed *cis* and *trans* dimers **I** and **II**, respectively.

Schmeme 3



ACKNOWLEDGMENT

This work was supported by a grant (# RO1 CA71079) from the National Institutes of Health.

REFERENCES

1). Allsebrook, W. E; Gulland, J. M.; Story L. F., "The Constitution of Purine Nucleosides. Part X. A New Synthesis of Xanthineand Attempted Synthesis of Xanthine Glucosides and Glyoxalines," *J. Chem. Soc.* **1942**, 232-236.

2). Hosmane, R. S.; Bhan, A., "The Synthesis of Ring-expanded Analogues of Xanthine, Containing the Imidazo[4,5-*e*][1,4]diazepine Ring System," *J. Heterocycl. Chem.* **1990**, *27*, 2189-2196.

3). Vaidya, V. P.; Hosmane, R. S.; Siriwardane, U.; Zhang, H.; Hosmane, N. S., "Unequivocal Structural Assignment of the Product of Methylation of 4-Nitro-5-styrylimidazole," *Struct. Chem.***1993**, *4*, 339-343.

4). Vaz, A. D. N.; Schoellmann G., "A Convenient and Simple Method for '-Chlorination of , and Conjugated Ketones," *J. Org. Chem.* **1984**, *49*, 1286-1288.

All comments on this poster should be sent by e-mail to (mailto:ecsoc@listserv.ariz ona.edu) ecsoc@listserv.arizona.edu with **A0030** as the message subject of your e-mail.
