Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 6965–6967

TETRAHEDRON
LETTERS

The formation of medium-sized rings by the intramolecular cyclization of arylnitrenium ions

Rudolph A. Abramovitch,[a,*] Joseph Miller[b,†] and Antonio J. C. de Souza[b]

[a] *Department of Chemistry, Clemson University, Clemson, SC 29634-0973, USA*
[b] *Universidad Estadual de Campinas, Campinas, SP 13100-000, Brazil*

Received 2 June 2003; revised 23 June 2003; accepted 23 June 2003

Abstract—The synthesis of an aminodibenzo[*a*,*c*]octadiene and an aminodibenzo[*a*,*c*]octatriene, guided by molecular mechanics calculations, was effected by the intramolecular cyclization of the corresponding open chain nitrenium ions. Also reported is the predicted failure to synthesize another aminodibenzo[*a*,*c*]octadiene using this method.

Intramolecular cyclizations of arylnitrenium ions have led to a variety of important ring systems resulting from C–C, N–C, and C–O bond formation. Thus, 9,10-dihydroaminophenanthrenes and a phenanthrene 9-carboxylate,[1] isoquinoline alkaloids,[2] 4-aminobenzo[*c*]chroman,[3] a dihydrophenanthridine,[3] 2-aminodibenzocycloheptadiene,[4] 3-amino-6,7-dihydro-5*H*-dibenzo[*a*,*c*]cycloheptadienone and a trifluoromethanesulfonyl enolate derivative (the latter incorporating 1,2,3-trimethoxy groups) obtained in low to modest yields,[4] all resulting from intramolecular C–C bond formation, pyrimido[4,5-*b*]indoles,[5] a 16-membered aporphine-based ring system[6] (both formed by N–C bond formation), and a variety of lactones,[7] resulting from O–C bond formation, among many others, were synthesized in this way.

We now report the preparation of a new aminodibenzo[*a*,*c*]octadiene and a related dibenzocyclooctatriene, whose formation were predicted by MMX calculations on model precursors, and the failure of an intramolecular cyclization, also predicted by such simple calculations. There are a number of conformations with slightly higher energies (within <1 kcal) than the computed global energy minimum one, which are close in geometry to the GMMXE conformation. To really predict the cyclization rate one would have to evaluate the relative populations of all the low energy minima. It seems, however, that the MM global energy minimum conformation has some predictive value as regards the feasibility of intramolecular cyclization.

The starting material for the dibenzooctadiene was 1-(3-azidophenyl)-4-phenylbutane (**1**) which was synthezised as shown below:

$$\textit{trans}\text{-PhCH=CHCHO} \xrightarrow{\text{NaBH}_4} \text{PhCH=CHCH}_2\text{OH} \xrightarrow{\text{SOCl}_2\text{/ Py}} \text{PhCH=CHCH}_2\text{Cl} \xrightarrow[\text{(ii) NaOMe}]{\text{(i) PPh}_3}$$

$$\xrightarrow{\text{(iii) }\underline{\text{m}}\text{-nitrobenzaldehyde}} \text{PhCH=CH-CH=CH-C}_6\text{H}_4(\underline{\text{m}}\text{-NO}_2) \xrightarrow{\text{(i) [H]}} \xrightarrow[\text{[iii] NaN}_3]{\text{(ii) NaNO}_2\text{/H}^+} (\mathbf{1})$$

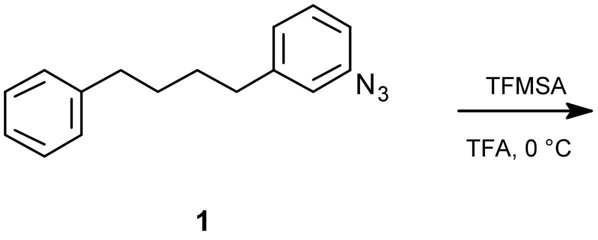
Keywords: nitrenium; intramolecular cyclizations; medium-sized rings; MMX.

* Corresponding author. Tel. +1-864-656-5008; fax: +1-864-656-6613; e-mail: raa@clemson.edu

† Present address: Universidade Federal da Paraiba, Laboratorio de Tecnologia Farmaceutica, Campus Universitario, Caixa Postal 5009, 58051-970, Joao Pessoa, Brazil.

0040-4039/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/S0040-4039(03)01591-0

A shorter route starting with *m*-nitrophenyl triphenylphosphonium bromide and cinnamaldehyde resulted in a lower overall yield of product owing to the low yield of Wittig product formed. Treatment of **1** with a few drops of trifluoromethanesulfonic acid in trifluoroacetic acid solution at 0°C gave a 28% (after purification) of 3-aminodibenzo[*a*,*c*]octadiene (**2**)



The low yield of intramolecular cyclization product is in complete agreement with the earlier result from the cyclization of 1-(4-azidophenyl)-4-phenylbutane to give a compound in 1% yield to which structure **3b** was assigned (a trace of material to which structure **3a** was assigned and was only detectable by GC/MS).[8] Owing to the trace quantities obtained, no spectroscopic studies other than the mass spectrum were obtained at the time. It seems more likely to us now in retrospect that the compounds were the C–C intramolecular cyclization products **3c**. The global minimum energy conformation of the model for the nitrenium ion leading to putative compounds **3** [1-(4-nitrophenyl)-4-phenylbutane: there are no MM parameters for the nitrenium group,[9] so we used the strong electron-withdrawing nitro group instead] is the 'linear' conformation. A somewhat bent conformation lies about 1 kcal above the global energy minimum conformation, and the computed distance between two of the *ortho* groups in the two rings is 6.753 Å (see Fig. 1). On the other hand, the global energy minimum conformation of 1-(3-nitrophenyl)-4-phenylbutane is slightly bent (Fig. 2), and the predicted distance between the carbon *para* to the nitro group and an *ortho* carbon in the other aryl group is 4.409 Å, close enough that some intramolecular C–C bond formation might be expected. This was indeed the case, and **2** was obtained in 28% yield after column chromatography. The other tarry products eluted could not be identified.

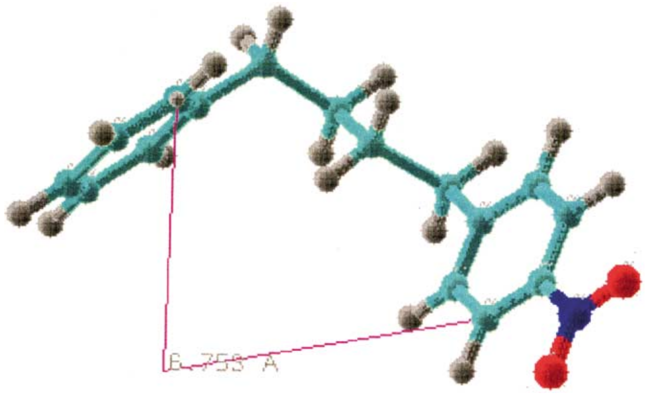


Figure 1. MMX bent conformation of 1-(4-nitrophenyl)-4-phenylbutane.

A much better source of aminodibenzo[*a*,*c*]octatriene (and eventual octadienes via the reduction of the triene) derivatives is azide **5**. MMX calculations indicated that the predicted distance between the vacant position *para*

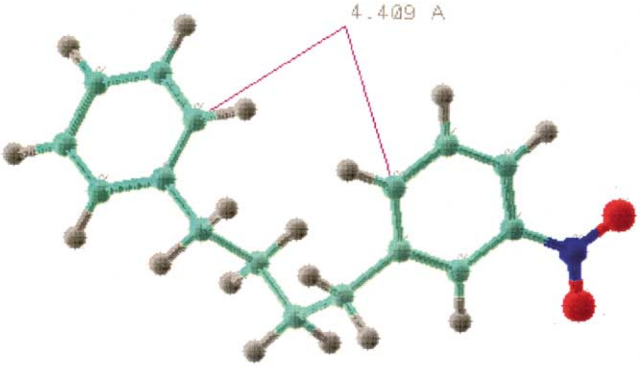


Figure 2. MMX global energy minimum conformation of 1-(3-nitrophenyl)-4-phenylbutane.

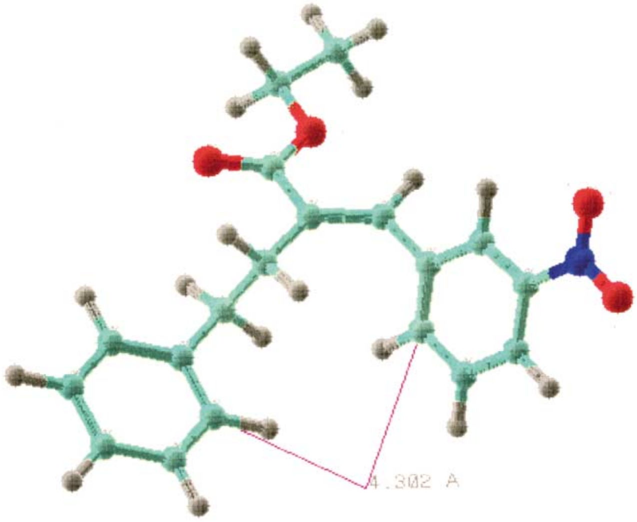
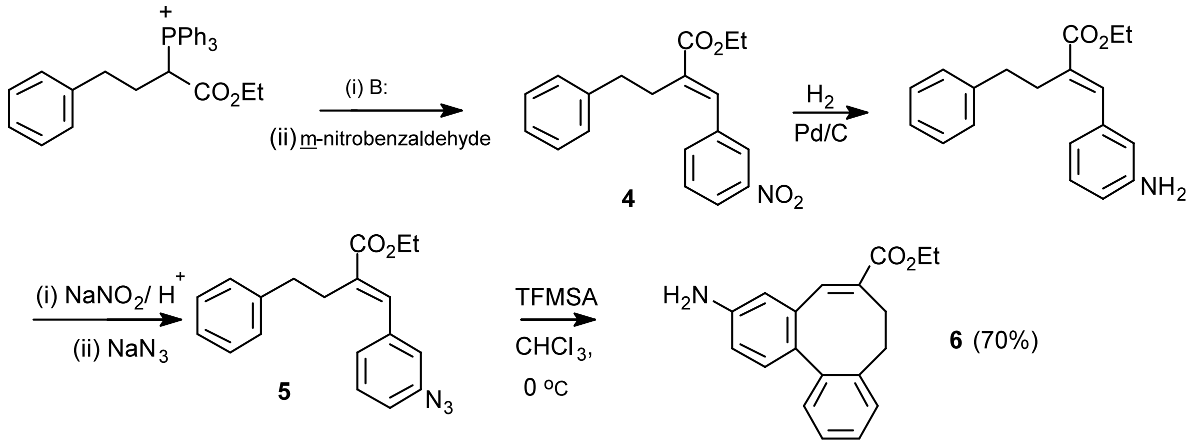


Figure 3. MMX global energy minimum conformation of **4**.



Scheme 1.

to the nitro group and one of the *ortho* positions of the phenyl group is 4.299 Å (Fig. 3). In addition, of course, the alkene group imparts some rigidity to the chain, which is lacking in the precursor to **2**. Azide **5** was synthesized as shown in Scheme 1. Generation of the nitrenium ion with TFMSA at 0°C gave a 70% yield of **6**. The latter's functionalities would permit the synthesis of a wide variety of substituted dibenzo-[*a*,*c*]cycloheptatrienes.

1-(3-Azidophenyl)-2,2-dicarbethoxy-4-phenylbutane (**7**) was synthesized from diethyl 2-phenethylmalonate and 3-nitrobenzyl bromide, followed by reduction of the nitro- to amine and thence to the azide, which would serve as a precusor to 3-aminodibenzo[*a*,*c*]-cyclooctadiene diethyl carboxylate if the conformation of the nitrenium ion was suitable to achieve ring-closure. The global energy minimum conformation (MMX) of the nitro precursor **8** is shown in Figure 4, which predicts that no intramolecular cyclization would take place. In actual practice, the only pure product from **7** obtained on treatment with TFMAS at 0°C and isolated by column chromatography was trifluoromethylsulfonate **9** (35% yield), resulting from the nucleophilic addition of $CF_3SO_2O^-$ to the arylnitrenium ion. Such 'undesired' products have been reported before.[4,7,10] These reactions may be viewed as the introduction of a protected hydroxyl group into an aniline ring system, and as such may be useful.

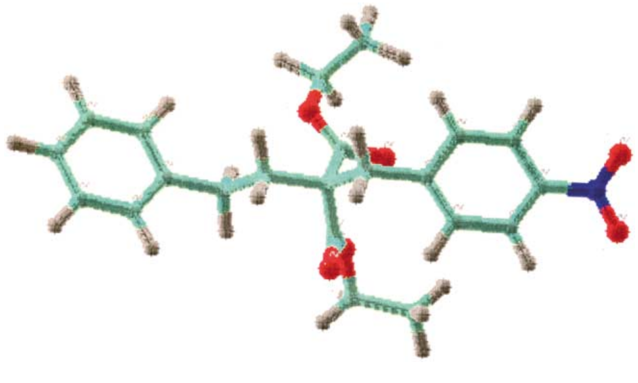


Figure 4. MMX global energy minimum conformation of **8**.

References

1. Abramovitch, R. A.; Cooper, M.; Iyer, S.; Jeyaraman, R.; Rodrigues, J. A. R. *J. Org. Chem.* **1982**, *47*, 4819.
2. (a) Kametani, T.; Takahashi, K.; Ogasawara, K.; Chu, V. L.; Fukumoto, K. *Collect. Czech. Chem. Commun.* **1975**, *40*, 712; (b) Abramovitch, R. A.; deSousa, J. D. F.; Rodrigues, J. A. R. *J. Am. Chem. Soc.* **1994**, *116*, 9745.
3. Abramovitch, R. A.; Cooper, M.; Jeyaraman, R.; Rusek, G. *Tetrahedron Lett.* **1986**, *27*, 3705.
4. Abramovtich, R. A.; Jeyaraman, R.; Yannakopoulou, K. *J. Chem. Soc., Chem. Commun.* **1985**, 1107.
5. Hyatt, J. S.; Swenton, J. S. *J. Org. Chem.* **1972**, *37*, 3216.
6. Abramovtich, R. A.; Chinnasamy, P.; Evertz, K.; Huttner, G. *J. Chem. Soc., Chem. Commun.* **1989**, 3.
7. Abramovitch, R. A.; Hawi, A.; Rodrigues, J. A. R.; Trombetta, T. R. *J. Chem. Soc., Chem. Commun.* **1986**, 283.
8. Abramovitch, R. A.; Shi, Q. *Heterocycles* **1994**, *38*, 2147.
9. The electron-withdrawing nitro group is used as a substitute for the nitrenium ion group since parameters for the latter are not available in MMX.
10. Abramovitch, R. A.; Rauter, A. P.; da Silva Pinto, O., 2002, unpublished results.