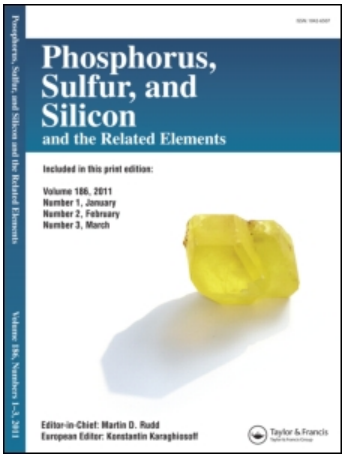

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Attempted Synthesis and Theoretical Calculations of the Elusive Polycyclic Arene Episulfides

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ATTEMPTED SYNTHESIS AND THEORETICAL CALCULATIONS OF THE ELUSIVE POLYCYCLIC ARENE EPISULFIDES

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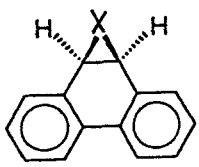
Abstract In pursuit of the thus far illusive polycyclic arene episulfides (PAE) — as model compounds for further study in relation to chemistry-based cancer research — we have attempted the synthesis of phenanthrene episulfide by using phenanthrene oxide, phenanthrene, and 5,7-dihydrodibenzo[c,e]thiepin as key starting materials. Following preliminary theoretical calculations of the targeted PAE's, the synthesis of 9,10-episulfide-trans-7,8-dihydroxy-7,8-dihydro[a]pyrene has been initiated. Our results indicate that apparently the elusive phenanthrene episulfide has been formed through the use of selected sulfur transfer agents, but the conditions to avoid its desulfurization should be worked out.

INTRODUCTION

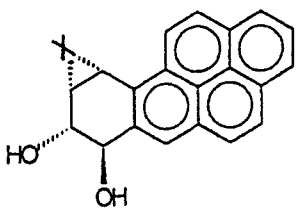
Epoxides such as 1a are the primary metabolites of PAHs and their further metabolites, the diol epoxides such as 2a, are considered to be the ultimate carcinogenic metabolites.[1] The synthesis of such metabolites has played an important role in cancer-related chemical research[1], and, indeed, a great number of polycyclic arene epoxides and diol epoxides[1,2] have been synthesized and extensively studies[1,3].



1

a. X=0

b. X=S



2

a. X=0

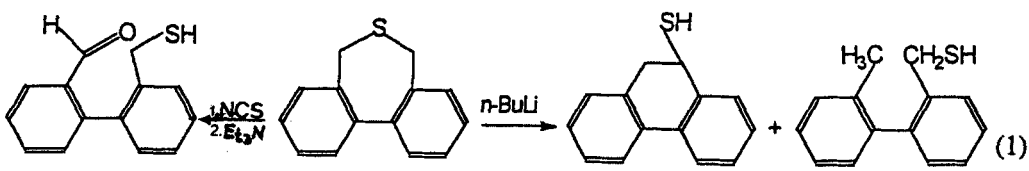
b. X=S

Surprisingly, however, their sulfur analogs, e.g. polycyclic arene episulfides such as 1b and 2b are unknown thus far,[4] and they form the subject of this communication. Our research involved the attempted synthesis and theoretical calculations of the hitherto unknown nonfunctionalized and functionalized K- and Bay-region polycyclic arene episulfides (PAEs), — the sulfur-analogs of the arene epoxides — in relation to chemistry-based cancer research.

In view of the continuing interest in the polycyclic aromatic hydrocarbons[5-6] in general, and the 'ultimate' 2,3-dihydroxy epoxide carcinogens (e.g.2a) in particular[7-8] we believe that our study, if successful in making some PAEs available synthetically, may open the gate for a new area of PAH cancer-related research.

RESULT AND DISCUSSION

Our first synthetic target has been the phenanthrene episulfide 1b, the synthesis of which was attempted starting with thiepine 3 or via the reaction of either 1a or phenanthrene itself with appropriate sulfur transfer agent under mild conditions. The results are summarized below.

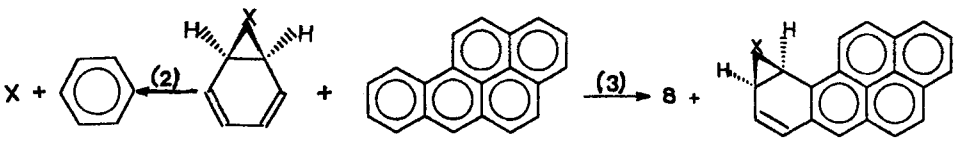


6 (~10%) 3 (12%) 4 (22%) 5 (1)

Since the reaction of bis(trimethylsilylsulfide) with bromine both in and without the presence of phenanthrene afforded elementary sulfur, the targeted phenanthrene episulfide is apparently not formed. On the other hand, NMR monitoring of the reaction of the epoxide 1a with the sulfur transfer agent 3-methyl-benzethiazole-2-thione under acidic conditions revealed the following spectrum: δ-7;21-8.73 (m, arom.), 6,37 (d), 5.50 (d),

3.93(s), 3,83 (s,3H,CH_3). By comparing these data with that obtained in previous attempts to synthesize 1b[9] the singlet at 3.93 is tentatively assigned to the corresponding episulfide.

Selected results of the semi empirical and *ab initio* calculations[10] of the energy of the reactions (2) and (3) on different levels of theory are given in table 1.



8 7 9 10

X=O,S

TABLE I. ΔG for reaction (2) and ΔH for Reaction (3) (Kcal/mole)

Reaction	X=	MP3/6-31G*‖6-31G*	PM3	AM1
2	O	32.19	48.56	44.77
2	S	9.44	18.44	16.67
3	O	—	-8.26	-7.42
3	S	—	-6.39	-7.52

Reaction 2 is calculated to be endothermic in all cases, the arene episulfides being considerably *less stable.* The small absolute value for the change in free energy in reacting 2 (for X=S), suggest that 7 would not be isolable at room temperature. Since the relative stabilities of the already known arene oxides would be a good indication for the probability to isolate the corresponding arene episulfides, these calculations predict the polycyclic arene episulfides (e.g. 1 and 10) have a good chance for being synthesized. Consequently the synthesis of 10 (X=S) has been initiated using "classical" methods[7] and it is currently in progress.

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