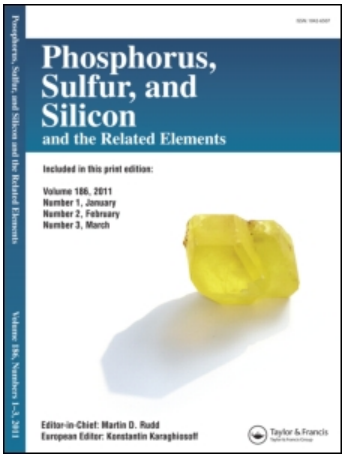

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Preparation methods of dibenzoxanthene derivatives are surveyed alongside the synthesis of some of the titled compounds, which are the sulfur analogues of dibenzoxanthenes. Our new procedure for the conversion of phenols to thiophenols was used to prove the structure of such sulfur analogues.

Keywords 2-naphthalenethiol; 2-naphthalenol; aldehydes; anthracene; microwave assisted reaction; thiadibezoanthracene

INTRODUCTION

Dibenzoxanthene derivatives have been the subject of many research works because of their importance in organic synthesis and as candidates in Photodynamic therapy (PDT).[1] [PDT uses nonthermal lasers to activate light-sensitive drugs [photosensitizers] in order to treat cancer and other diseases in a nonsurgical, minimally invasive way. PDT photosensitizers are injected directly into malignant tissue and, when activated by a light source, generate highly reactive oxygen radicals that react with crucial cell biochemicals, such as proteins and DNA, damaging them beyond repair and killing the tumor cells].

As concerning the parent compound **3** (Scheme 1) many authors have attempted the synthesis of R = H (abbreviated as dibenzoxanthene). For example, Wolf has dehydrated bis(2-hydroxy-1-naphthyl)methane **2**, R = H (which we abbreviate here as bisnaphthol) by $POCl_3$.[2] Rosenbush has proposed another way to dibenzoxanthene by boiling acetic acid diester of compound **2**.[3] Casiraghi and colleagues have prepared **3**, R=H and its 2,12-dibromo-derivatives by refluxing magnesium salts of the corresponding 2-naphthalenols in ethyl orthoformate.[4] Dimerization of

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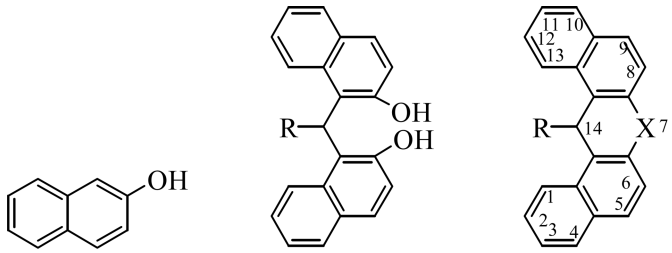


1 **2** **3,** X= Oxygen
4, X= Sulfur

SCHEME 1

2-naphthalenol under CO—CO_2 flow also has been attempted by Ohta and colleagues to prepare dibenzoxanthene in a 35% yield.[5] In the other method of preparing dibenzoxanthene, use has been made of a two-step addition of HCO_2NH_4 to **1** at 190–200°C.[6]

Recently we reported that 14-alkyl-14*H*-[a,j]dibenzoxanthenes **3**, R=Alkyl (abbreviated here as alkyldibenzxanthenes) may be prepared without further purification by condensation of 2-naphthalenol **1** and unhindered aliphatic aldehydes in acetic acid (as a solvent) and a catalytic amount of concentrated HCl or H_3PO_4 at 0–5°C.[7] There also is a recent report in which 14-ethyl substituted dibenzoxanthene were prepared in a 31% yield by condensing **1** and propanal at high pressure.[8] Benzyldibenzoxanthene (**3**, R = $C_6H_5CH_2$) has been prepared by passing gaseous HCl through a concentrated acetic acid solution for two hours.[9] In another report, propyldibenzoxanthene (**3**, R = $CH_3CH_2CH_2$) has been obtained by boiling a mixture of **1** and butanal in HCl/acetic acid.[10]

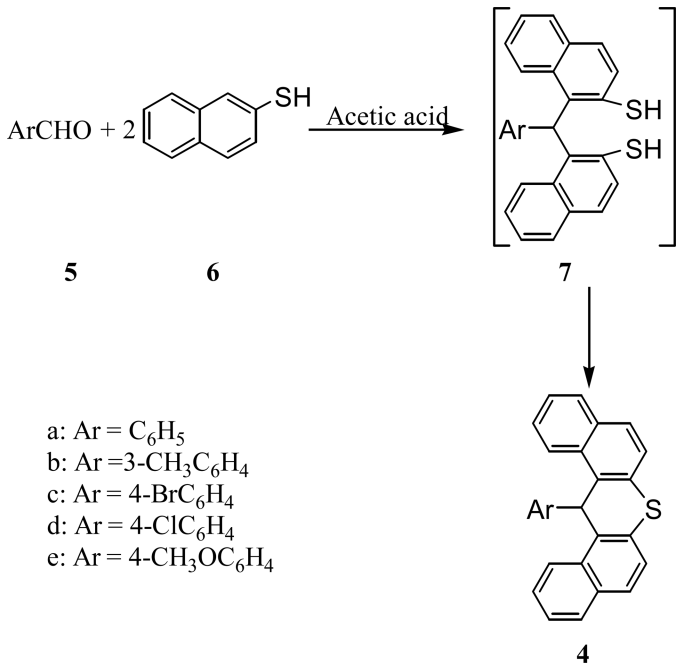
The case of 14-aryl-14*H*-[a,j]dibenzoxanthenes **3**, R = Aryl (abbreviated here as aryldibenzoxanthenes) is similar to that of alkyldibenzoxanthenes. They have been prepared through dehydration of their corresponding bisnaphthols **2**,[11] or by boiling a mixture of aromatic aldehydes and 2-naphthalenol in HCl/acetic acid.[12] There also is a report on room temperature preparation of such compounds from the starting materials in acetic acid by adding concentrated HCl.[13]

Despite the above-mentioned methods for the preparation of dibenzoxanthenes, the literature survey shows that there is no report on the synthesis of their sulfur-containing analogues, though Akar and his colleagues have reported the condensation of dialdehydes and 2-thionaphthol to prepare dinaphthodithiocine.[14]

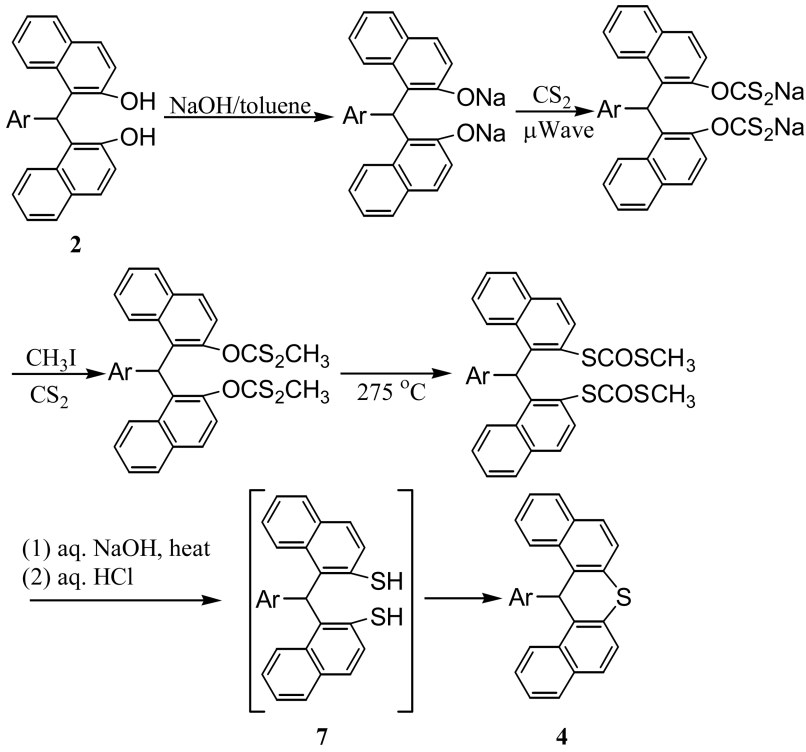
RESULTS AND DISCUSSIONS

The condensation of 2-naphthol and aromatic aldehydes in acetic acid and a few drops of HCl mainly yields bisnaphthol derivatives, which may be converted to the corresponding dibenzoxanthenes by dehydration. The reaction of 2-thionaphthol **6** with the same aldehydes **5** in acetic acid (without addition of HCl), in contrast, proceeds to give sulfur-containing analogues of dibenzoxanthene **4** directly even at low temperatures (in an ice bath). This reaction is completed after one hour. It is plausible that the reaction proceeds through bisthionaphthols **7** (Scheme 2).

The chemical identity of the reaction product **4** was confirmed when the corresponding bisnaphthols **2** were subjected to our developed procedure for the conversion of phenols to thiophenols. In this procedure (which will be fully described for the conversion of phenol to thiophenol in experimental section), the same products are formed (Scheme 3), though in lower yields (about 49–50%). (In this procedure, precautions must be taken to prevent overheating of carbon disulfide: it is volatile and flammable.)



SCHEME 2



SCHEME 3

Table I shows the result of condensation of aromatic 2-naphthalenethiol **6** and aromatic aldehydes (Scheme 2). Product yields in Table I are good (>84%).

A surprising, and at present, unexplainable behavior of 2-thionaphthol is that it does not undergo a condensation reaction with aliphatic aldehydes even after a few drops of HCl are added to acetic

TABLE I Melting Points for Product 4 (See Scheme 2)

Entry	**5**, ArCHO	Product	M.p.°C
1	**5a**	**4a**	140
2	**5b**	**4b**	132
3	**5c**	**4c**	122
4	**5d**	**4d**	99.3
5	**5e**	**4e**	94

acid under refluxing conditions. This is the case where the reaction of unhindered aliphatic aldehydes and 2-naphthol proceeds and completes at 0–5°C under the same conditions.[7]

Therefore, we have not only prepared aryl dibenzothioanthracenes but we also have developed a new low-cost procedure for the conversion of phenols to thiophenols. It is noteworthy that thiophenols may be prepared by the Newman-Kwart rearrangement,[15–16] which has been addressed by many researchers for the synthesis of arylthiols, including two recent reports.[17,18] However, they have used the moisture sensitive reagent N,N-dimethylthiocarbamoyl chloride which requires absolutely dry conditions.

EXPERIMENTAL

In this section, preparation of the compound **4e** and the conversion of phenol to thiophenol are fully described (alongside with their spectral data when necessary).

(1) Preparation of 14-(4-Methoxyphenyl)-14H-7-thiadebenzo[*a,j*]anthracene, 4e

To a magnetically stirred and cold solution of 2 mmol (0.16 g) of 2-naphthalenethiol in acetic acid, is added 1 mmol (0.12 mL) of 4-methoxybenzaldehyde. The reaction is completed after 1 h.

90MHz ^{1}H NMR ($CDCl_3$): δ 3.73 (3H, MeO); δ 5.64; δ 6.74–7.81 (18H, aromatic).

90MHz ^{13}C NMR ($CDCl_3$): δ 57.044; δ 61.762; δ 115.822; δ 128.198; δ 128.303; δ 129.441; δ 129.526; δ 130.197; δ 131.069; δ 131.377; δ 133.356; δ 133.488; δ 134.032; δ 134.403; δ 135.402; δ 161.482.

(2) Conversion of Phenol to Thiophenol

(a) Preparation of Sodium Phenoxide

50 mmol phenol (4.7 g) is dissolved in 25 mL of toluene. To this solution, 50 mmol (2.0 g) of sodium hydroxide is added and stirred for 30 min. The precipitate (sodium phenoxide) is separated and dissolved in CS_2.

(b) Preparation of S-sodium O-phenyl Dithiocarbonate

The above solution is subjected 15 times, and each time for 1 minute, to 100% of power of our domestic microwave oven (LG Microwave Oven MG-583MC). To prevent ignition of CS_2 vapors during irradiation, the

reaction vessel is closed and after each one-minute period the solution is allowed to cool.

(c) Preparation of S-Methyl O-Phenyl Dithiocarbonate

To the resulting CS_2 solution, which contains S-sodium O-phenyl dithiocarbonate, 50 mmol of iodomethame is added and refluxed for 1 h with stirring. The CS_2 solvent is removed to obtain a white powder, which is used without further purification.

(d) Preparation of Diphenyl Disulfide

S-methyl-O-phenyl dithiocarbonate is first rearranged to its isomer, S-methyl-S-phenyl dithiocarbonate, by heating the white powder at 275°C under nitrogen gas for 1 h. S-methyl-S-phenyl dithiocarbonate is then hydrolyzed by adding 10% aqueous sodium hydroxide to a cooled reaction mixture and is refluxing for 30 min. An addition of dilute HCl converts the hydrolyzed product (C_6H_5SNa) to thiophenol. However, direct separation of thiophenol from this reaction mixture is practically impossible. Therefore, it is first oxidized in situ by trichloroisocyanuric[19] acid in CH_2Cl_2 to diphenyl disulfide ($C_6H_5SSC_6H_5$), which is then washed with 5% sodium hydroxide to remove any trace of unreacted phenol. The solvent is removed to obtain diphenyl disulfide as a white powder.

(e) Preparation of Thiophenol

The above diphenyl disulfide is reduced by zinc/acetic acid. Thiophenol is then separated by conventional methods, the melting point and spectral data of which are consistent with the reported ones. Yield: 42%.

Note 1: All steps are carried out in a good ventilated hood.

Note 2: Oxidation-reduction steps are not necessary for the conversion of bisnaphthols to 14-aryl-14*H*-7-thiadibenzo[*a*,*j*]-anthracenes.

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