

This invention relates to an improved process for the preparation of **Naptho [1,8-cd] dithiole**. More particularly, the present invention relates to an improved process for the preparation of Naptho [1,8-cd] dithiole from **1,8-diamino** naphthalene in two simple organic transformations.

Substituted **naphtho** [1,8-cd] dithiole has been used as an antiviral agent (**Jpn. Kokai Tokkyo Koho** Jp. 0803,039, CA 124, 220499q, 1996). It also has been used for the protection of **aldehydes** and ketones (Compt. Rend, 152, 92-94, 1911. Fr). These protected aldehydes and ketones can be easily deprotected to regenerate them in high yields without the use of either the unpleasant smelling **alkylthiols**, or heavy metals or strong acids. Recently it has been found that naphtho [1,8-cd] dithiole has the capability to form **redox** active self-assembled **monolayer** on gold (**Langmuir** 13, 866-869, 1997)

Like **aromatic sulfides** in **general**, naphtho [1,8-cd] dithiole is a bright red crystalline substance and possesses an **anomolously** deep color for such a simply constructed compound [**Ref:** (1) H.S. **Desai** and B.D. **Tilak**, J.Sci **Ind.** Res. (India) 19B, 390 1960); Compt. Rend 152 92-94 (Fr) (1911); W.B. Price and S. Smiles, JCS 2372, (1928)]. Attempts to explain this **effect** theoretically by means of the dipole moment method or **UV** and **IR** spectroscopy [Ref. H.S. **Desai** and B.D. **Tilak**, J.Sci Ind. Res. (India) 19B, 390 (1960)] led to the conclusion that a necessary condition for the deep color **of** this compound is the **coplanarity** of the S-S group and the  $\pi$  electron system of the naphthalene. A consequence of this could be 3p-3d overlap of the unshared electrons of the adjacent sulfur atoms or interaction of the 3p electrons of one sulphur atom with the 3d orbital of the adjacent sulfur **atom**. Data from the quantum chemical character also indicates strong **delocalization** of the 3p electrons of the S-S group and the formation of a general  $\pi$  electron **system**.

In the prior art, the synthesis of naphtho [1,8-cd] dithiole has known to be achieved by several methods. In most of them, **1-naphthylamine-8-sulfonic acid** is used as the starting material. In one of the method [W.B. Price and S. Smiles, JCS 2372, (1928)], **1-naphthylamine 8-sulfonic acid** was treated with nitrous acid and then with **sulfurous acid** in presence of copper. The **1-sulphinonaphthalene-8-sulfonic acid** so obtained was subjected to reduction in aqueous solution with sulfurous acid and dilute **hydroiodic acid** affording the corresponding **1,1'-dithionaphthalene-8,8'-disulfonic acid**. Treatment of the chloride of this acid in the usual way gave **1,1'-dithionaphthalene 8,8' -disulphonic acid** which finally was reduced to the required **1,8-dithiol naphthalene**. This unstable **mercaptan** on exposure to air or in solution with mild oxidizing agent yielded the orange **disulphide** in overall yield of 21% [JOC 30(12), 3997-4001 (1965)].

In yet another method [H.S. Desai and B.D. Tilak, J.Sci Ind. Res. (India) 19B, 390 (1960)], **1-aminonaphthalene-8-sulfonic acid** was **diazotized**, then treated with potassium ethyl **xanthate** and saponified with caustic **alkali**. The resulting **dipotassium salt of disulfodinaphthyl disulfides** are converted by treatment with **PCl<sub>5</sub>** and phosphorous **oxychloride** into **dinaphthyl disulfide disulphonchloride** which on reduction with **zinc** dust and hydrochloric acid is converted into **1,8-dimercaptonaphthalene**. Aeration with **ammoniacal ethanol** gave **naphtho [1,8-cd] dithiole** in an overall yield of 30%.

In another method from **periacid (1-naphthylamine-8-sulfonic acid** [A Zweig and A.K. Hoffman JOC Vol. 30, 12, 3997-4001 (1965)] after five tedious steps, a 21% overall yield of **1-naphtho [1,8 cd] dithiole** was obtained.

In yet another process (M. Jerrold, D. David, J.J. Hanser, JACS 99(1) 255-7 (1997)) unstable 1,8 **dilithionaphthalene** was treated with sulfur in dry THF at -78°C to give 35-40% yield of the product.

In yet another highly moisture sensitive synthesis [M. Jerrold, D. David, J.J. Hanser JACS 99(1) 255-7 (1997)] **8-chloro 1-naphthalene thiol** was treated with 2-**equiv** of **n-butyl** lithium in dry THF at 25°C to generate an intermediate **dithiosalt** which after reaction with elemental sulfur and subsequent **workup** gave the product in 44% yield.

In yet another process **1,8-dichloronaphthalene** with sodium **disulfide** in **hexamethylphosphoric triamide (HMPA)** gave 46% yield of naphtho- [1,8-cd] 1,2-**dithiole**.

Although **all** the variety of methods mentioned above in the prior art are known to be useful for the preparation of naphtho [1,8-cd] 1,2-dithiole, they suffer from the following drawbacks:

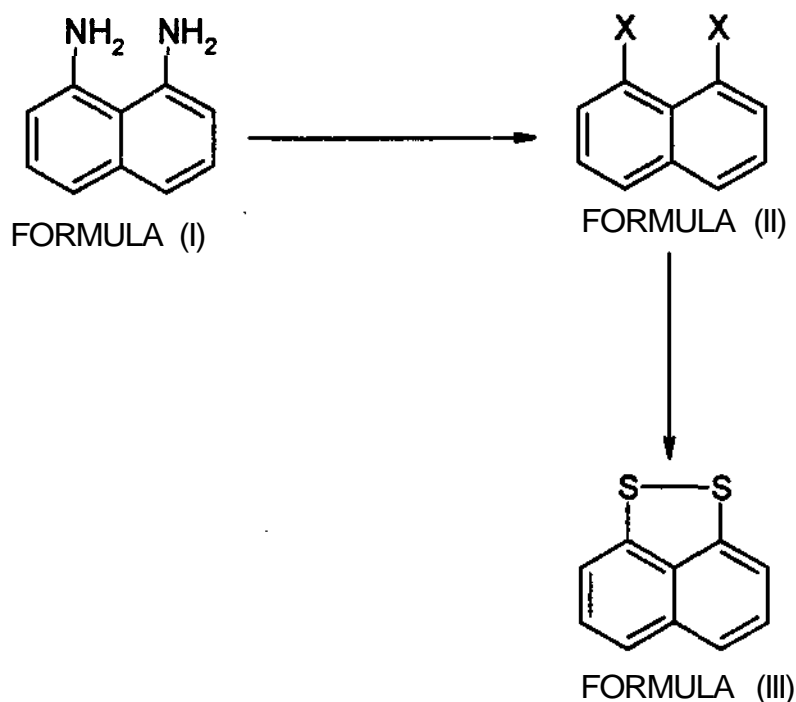
1. It has been found that there is no method reported for the conversion to naphtho [1,8-cd] **dithiole** from **1,8-diamino** naphthalene in good yield and purity.
2. The reported methods from **1-naphthylamine 8-sulfonic** acid involve **multisteps** with lowered yields and purity of final product.
3. Many of the reagents required for the reported methods involve expensive chemicals and moisture sensitive reagents posing material handling problems in large-scale operations.
4. Most of the reactions involve low temperatures like -78°C.
5. The reaction procedures are complicated and work up procedures are lengthy and tedious.

6. These reported procedures are not cost **effective**.

In view of all the above disadvantages of the prior art, it was desirable to develop a convenient process for the preparation of **naphtho [1,8-cd] dithiole** in good yield and purity from easily accessible raw material.

The object of the present invention to provide a process for the preparation of **naphtho [1,8-cd] dithiole** from easily available materials like **1,8-diamino** naphthalene by employing mild reaction conditions like **diazotization** and **sulfurization**.

The **present** invention provides a process for preparation of naphtho [1,8-cd] of formula (III) by **diaminonaphthalene** with a **diazotizing** agent to obtain **dihalo** derivative of naphthalene of formula (II) which is further treated with sulphur in **presence** of an aprotic solvent to get the product.



Accordingly the present invention provides an improved process for the preparation of naphtho [1,8-cd] dithiole which comprises, treating 1,8-**diaminonaphthalene** with diazotizing agent in acidic medium in the presence of **antifroth** agent at a temperature in the range of  $-20^\circ\text{C}$  to  $30^\circ\text{C}$  and treating this

mixture with copper or potassium halide in presence of a corresponding halo acid to obtain dihalo derivative, refluxing the mixture with sulphur in presence of an aprotic solvent at a temperature in the range of 140 to 180°C for a period of 4 to 6 hrs, quenching with water and separating by conventional methods such as distillation, extraction or filtration to obtain naphtho [1,8-cd] dithiole.

In one of the embodiment of the present invention, the diazotizing agent used is a mineral acid solution of alkali metal nitrite.

In another embodiment, the mineral acid used is selected from sulphuric acid or hydrochloric acid preferably sulphuric acid.

In yet another embodiment the alkali metal nitrite used is selected from sodium nitrite, potassium nitrite and lithium nitrite, preferably sodium nitrite.

In yet another embodiment the antifoaming agent used is organic solvent ethyl acetate, benzene or n-butanol preferably n-butanol.

In still another embodiment the metal halide used is selected from copper and potassium halide preferably potassium halide.

In yet another embodiment the corresponding halo acid used is selected from hydrochloric acid, hydrobromic acid or hydroiodic acid.

In still another embodiment the aprotic solvent used is selected from the group consists dimethyl form amide (DMF), dimethyl sulphoxide, hexamethyl phosphoroamide, preferably DMF.

The process of the present invention is described herein below with reference to examples, which are illustrative only and should not be construed to limit the scope of the present invention in any manner.

**Example 1: This example illustrated preparation of 1,8-dichloronaphthalene**

1,8-diaminonaphthalene (1.6 g, 0.01 mol) was finely dispersed in hydrochloric acid (13 ml, 17%) and after cooling in ice bath and addition of ice (5 g) tetrazotized by sodium

nitrite (1.4 g, 0.02 mol) in water (5 ml). **n-Butanol** (2 ml) was added to prevent froth formation. The solution was poured into cuprous chloride (5 g, 0.05 mol) in **conc.** hydrochloric acid (20 ml). The mixture was slowly heated to boiling until benzene was distilled out and then steam distilled and the solid distillate triturated in cold with aqueous sodium hydroxide, filtered **off** and steam distilled again after addition of potassium hydroxide. The solid distillate was **recrystallized** from alcohol to afford colourless needles of **1,8-dichloronaphthalene** (0.9 g) in 45% yield.

**Example 2: This example illustrated preparation of 1,8-dibromonaphthalene**

A solution of **1,8-diaminonaphthalene** (6 g, 0.38 mol) in glacial acetic acid (50ml.) was stirred at 0°C into a solution of sodium nitrite (6 g, 0.087 mol) in **conc.** Sulphuric acid (50 ml.). After **1hr.** the mixture was poured into water (50 ml.) and mixed with chopped ice (100 gm.) and urea (**1g** .0016 mol) was added to remove excess of nitric acid. The **diazo-solution** was filtered and then added to the solution of cuprous bromide (5 g, 0.035 mol) in **hydrobromic** acid (75 ml., **d=1.7**) and water (25 ml.) to give **1,8-dibromo** naphthalene (6.5 g) in 60% yield.

**Example 3: This example illustrated preparation of 1,8-diiodonaphthalene**

1,8-diaminonaphthalene (83.3 g, 0.53 mol) in sulfuric acid suspension (975 ml, 6.9 mol) was cooled to -20°C and then a solution of sodium nitrite (105 g, 1.59 mol) in water (400 ml) was added **dropwise** under stirring maintaining the temperature of the reaction mixture at -15°C. As soon as the addition was complete, a solution of **KI** (538 g, 3.24 mol) in water (450 ml) was added dropwise under stirring keeping the reaction mixture at -15°C. An additional portion of **con.** sulfuric acid was added to keep the reaction mixture from freezing. It was warmed to 80°C, under stirring, cooled to 20°C and then made alkaline with aqueous sodium hydroxide. The mixture was filtered and the residue was extracted with ether. The ether extract was washed

successively with HCl (100 ml, 10%), saturated solution of  $\text{Na}_2\text{S}_2\text{O}_3$  in water and finally with NaOH (10%). The ethereal solution after drying with anhydrous  $\text{Na}_2\text{SO}_4$  and distillation to remove solvent gave 147.6 g crude product. This on recrystallization from hexane gave 1,8-diiodo naphthalene in 68% yield (m.p.  $110^\circ\text{C}$ ).

**Example 4 : This example illustrated preparation of Naphtho [1,8-cd] dithiole**

1,8-diiodo naphthalene (3.8 g, 0.01 mol) was dissolved in DMF (100 ml). To this was added sulfur (2.56 g, 0.01 mol). The solution was refluxed for 5h until 1,8-diiodonaphthalene had disappeared as monitored by TLC. The reaction mixture was cooled, poured in water (250 ml) and extracted with petroleum ether (4 x 50 ml). The petroleum ether extract was dried over anhydrous sodium sulfate and the solvent evaporated to give naphtho [1,8-cd] dithiole (1.81 g) in 95% yield.

**Example 5 : This example illustrated preparation of Naphtho [1,8-cd] dithiole**

1,8 dibromonaphthalene (2.86 g, 0.01mol.) was dissolved in DMF (50 ml.) and then sulphur (2.56 g, 1 mol) was added and refluxed for 5h. The reaction mixture was cooled to room temperature, poured into ice cold water (100 ml.), filtered to remove excess sulphur and then extracted with petroleum ether. The extract was dried over anhydrous sodium sulphate and solvent evaporated to afford naphtho [1,8-cd]-dithiole (0.38 g.) in 20% yield.

**Example 6: This example illustrated preparation of Naphtho [1,8-cd] dithiole**

1,8-dichloronaphthalene (1.96 g., 0.01 mol) was dissolved in DMF (100 ml.) and then sulphur (2.56 g., 1mol.) was added and refluxed for 5 hrs. The reaction mixture was cooled to room temperature and poured into ice cold water (500 ml.). The reaction mixture was filtered to remove the excess of sulphur, and then extracted with petroleum ether, dried over anhydrous sodium sulphate and solvent evaporated to afford naphtho [1,8-cd] dithiole (0.22 g.) in 12% yield.

### **The advantages of the present invention**

- 1) This is the first disclosure of the use of **1,8-diaminonaphthalene** to prepare **naphtho [1,8 cd] dithiole** in excellent yield and purity.
- 2) This is the first disclosure to prepare naphtho [**1,8-cd**] dithiole under moderate reaction conditions.
- 3) The products are pure enough and do not need further purification.
- 4) Almost quantitative yield of naphtho [1,8-cd] dithiole was obtained due to the peri-peri interaction of the iodo groups in **1,8-diiodo** naphthalene.
- 5) No sophisticated and moisture sensitive chemicals are used in the synthesis.
- 6) The process is cost **effective**
- 7) No side products are obtained in all the reactions.
- 8) The reactions are regioselective.
- 9) The reaction is very clean and work up involves minimum effort.