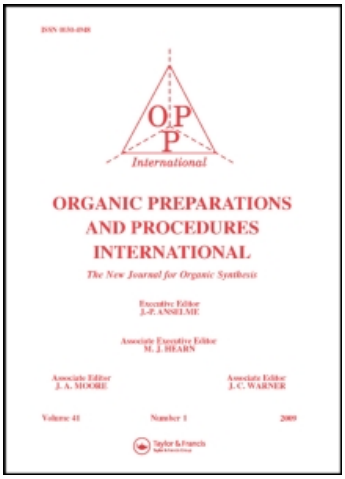


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

SYNTHESIS OF ACENAPHTHO[1, 2-b]BENZO[d]THIOPHENE

Gandhi K. Kar[a]; Basanta G. Chatterjee[a]; Jayanta K. Ray[a]
[a] Department of Chemistry, Indian Institute of Technology, Kharagpur, INDIA

To cite this Article Kar, Gandhi K. , Chatterjee, Basanta G. and Ray, Jayanta K.(1988) 'SYNTHESIS OF ACENAPHTHO[1, 2-b]BENZO[d]THIOPHENE', Organic Preparations and Procedures International, 20: 3, 213 — 222
To link to this Article: DOI: 10.1080/00304948809355813
URL: http://dx.doi.org/10.1080/00304948809355813

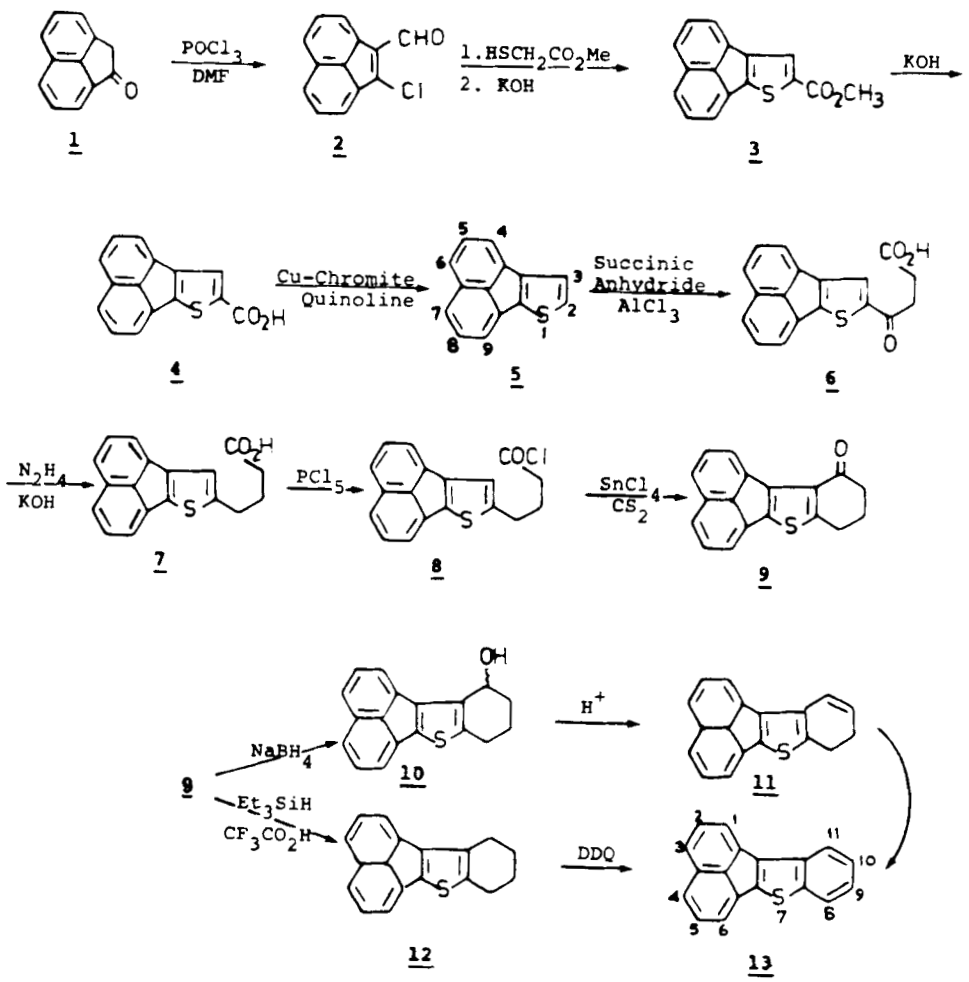
ORGANIC PREPARATIONS AND PROCEDURES INT. 20(3), 213-222 (1988)

SYNTHESIS OF ACENAPHTHO[1,2-b]BENZO[d]THIOPHENE †

Gandhi K. Kar, Basanta G. Chatterjee and Jayanta K. Ray*

Department of Chemistry
Indian Institute of Technology, Kharagpur 721 302, INDIA

The widely studied[1] isosteric relationship between benzene and thiophene has helped medicinal chemists to devise newer thiadrugs. The presence of polycyclic thiophene derivatives in polyaromatic hydrocarbons in coal-derived products [2] and shale oils[3] has elicited interest in this type of heterocycles. Although some data about the carcinogenic and mutagenic properties of some polycyclic thiophene derivatives is available[4], very little is known about the biological properties of natural thiophene derivatives, mainly because of the lack of materials isolated in pure condition. This has prompted many chemists to undertake the syntheses of various polycyclic thiophene derivatives[5]. We now describe an improved synthesis of the known[6] acenaphtho[1,2-b]thiophene (5) and its conversion to the hitherto unknown acenaphtho[1,2-b]benzo[d]thiophene (13) in nine steps. Thus acenaphthenone (1) was converted *via* a Vilsmeir-Haack reaction to the chloro aldehyde[7] (2) and then to 2-carboxy acenaphtho[1,2-b]thiophene (4) by the



condensation[8] of the chloro aldehyde with methyl thioglycollate in presence of Et_3N followed by saponification in 90% overall yield; this two-step reaction was preferable to the direct condensation of thioglycollic acid with chloro aldehyde (2). Decarboxylation of 4 in boiling quinoline with copper-chromite, afforded the acenaphtho[1,2-b]thiophene (5) in excellent yield.[6] Friedel-Crafts acylation of 5 with succinic anhydride in nitrobenzene at 0-5° afforded the ketocarboxylic acid 6 in 70% yield. Wolff-Kishner reduction[9]

of 6 followed by Friedel-Crafts cyclisation via the acid chloride gave 9. Acenaphtho[1,2-b]benzo[d]thiophene (13) was then obtained from ketone 9 by reduction to alcohol 10 followed by dehydration and finally aromatization to 13 in presence of DDQ in 90% yield. Alternatively, reduction of 9 to the tetrahydro derivative 12 with triethylsilane and trifluoroacetic acid[10] followed by aromatisation with dichlorodicyanoquinone(DDQ) gave the title compound in nearly quantitative yield.

EXPERIMENTAL SECTION

IR spectra were recorded on a Perkin-Elmer model 237B spectrometer. NMR spectra were recorded at 90 MHz on Varian EM 390 spectrometer using TMS as an internal standard.

2-Carbomethoxy Acenaphtho[1,2-b]thiophene (3).- To a stirred solution of the chloro aldehyde[7] 2 (1.1 g, 4.1 mmol) and methyl thioglycollate (0.7 g, 6.6 mmol) in 20 ml pyridine at 0^{o}, was added dropwise triethylamine (0.8 g, 7.9 mmol). The reaction mixture was stirred for 45 min. at 50-60^{o} and for 30 min. at room temperaure. An aqueous solution of KOH (2 ml, 48%) was added to the mixture and was stirred for 10 additional minutes. The reaction mixture was poured into ice water and extracted with chloroform. The organic layer was washed successively with dil. HCl and water, dried (Na_2SO_4) and the solvent was removed to yield 1.2g (91%) of 3 as yellow solid, mp. 141^{o} (EtOH). IR ($CHCl_3$) : 1700 cm^{-1}

($-CO_2CH_3$); nmr ($CDCl_3$) : δ 4.0 (s, 3H, CO_2CH_3), 7.6-8.0 (m, 6H, H_{4-9}), 8.1 (s, 1H, H_3); MS (m/e) : 266 (M^+), 235 (M-31, OCH_3), 207 (M-59, CO_2CH_3), 163 (M-103, CO_2CH_3, CS).

Anal. Calcd for $C_{16}H_{10}O_2S$: C, 72.18; H, 3.76

Found : C, 72.00; H, 3.65

2-Carboxyacenaphtho[1,2-b]thiophene (4).- To a solution of 3 (0.9 g, 3.6 mmol) in 50 ml of ethanol was added a solution of 0.7 g (12.5 mmol) of KOH in 25 ml of water. The mixture was refluxed for 5 hrs. After the removal of alcohol, the residue was diluted with water (100 ml), acidified (6N HCl). The precipitated acid was collected, washed (water) and dried to yield 0.9 g (100%) of 4, mp. 282° (benzene-methanol). IR (nujol) : 1675 cm^{-1} ($-CO_2H$); nmr (DMSO-d_6) : δ 7.6-8.0 (m, 6H, H_{4-9}), 8.1 (s, 1H, H_3); MS (m/e) : 252 (M^+), 235 (M-17, OH), 207 (M-45, CO_2H), 163 (M-89, CO_2H, CS).

Alternate Route to 4.- A mixture of 2 (0.6 g, 2.9 mmol), mercaptoacetic acid (0.4 g, 4.5 mmol) and sodium bicarbonate (0.7 g, 9 mmol) in ethanol (20 ml) was heated under reflux for 14 hrs. After removal of the solvent, the residue was dissolved in cold water and the neutral portion was separated out by extraction with ether. The organic layer was washed three times with water. The aqueous layer and washings of the organic layer were combined and acidified with conc. HCl. The solid was dissolved in ether, and the solution was washed with water, dried (Na_2SO_4) and evaporated. The residue was heated with aqueous solution of KOH (30%, 5 ml) on a water bath for 30 min and the mixture was diluted by 15-20 ml of

water and acidified (conc. HCl). The precipitated solid was collected and dried in air. Several crystallizations from benzene-methanol gave 4 as a yellow solid (0.4 g, 53%), mp. and mixed with previous sample mp. 281-282°.

Acenaphtho[1,2-b]thiophene (5).- A 0.2 g (0.79 mmol) sample of 4 was heated at reflux for 8 hrs. with freshly distilled quinoline (5 ml), and copper chromite (10-15 mg). After cooling, the catalyst was removed by filtration and the filtrate was poured on ice-cold conc. HCl and was extracted with ether. Removal of solvent after washing (H_2O) and drying (Na_2SO_4) furnished brownish yellow oil, which was passed through a short column of silica gel; elution with pet-ether (60°-80°) afforded 0.16 g (99%) of the title compound. mp. 73-74° (pet-ether 60°-80°), lit.[6] mp. 67°. IR ($CHCl_3$) : 1608 cm^{-1}; nmr ($CDCl_3$) : δ 7.3-7.9 (m, 8H aromatic).

Anal. Calcd. for $C_{14}H_8S$: C, 80.77; H, 3.85

Found : C, 80.62; H, 3.69

β-(2-Acenaphtho[1,2-b]theonyl)propionic acid (6).- To a stirred mixture of acenaphtho[1,2-b]thiophene 5, (1.1 g, 5.3 mmol) succinic anhydride (0.5 g, 5 mmol), in dry nitrobenzene (15 ml) at 0°, was added anhydrous $AlCl_3$ (1.6 g, 12 mmol) in three batches. Stirring was continued at 0-5° for 1.5 hr. and then at room temperature overnight. The mixture was then decomposed by addition to ice-water and nitrobenzene was removed by steam distillation. The yellow solid obtained was dissolved in hot conc. K_2CO_3 aqueous and was decolorized by

activated charcoal. Filtration of the mixture followed by acidification (6N HCl) afforded 6 as a yellow solid (1.1 g, 71%), mp. 222-223°. IR (Nujol): 1658 (C=O), 1700 (CO_2H) cm^{-1}; nmr (DMSO-d_6) : δ 2.85 (t, 2H, $\underline{CH_2}CO_2H$), 3.45 (t, 2H, $\underline{CH_2}CO$), 7.70-8.15 (m, 6H, H_{4-9}), 8.30 (s, 1H, H_3).

Anal. Calcd. for $C_{18}H_{12}O_3S$: C, 70.18; H, 3.90

Found : C, 69.95; H, 3.82

The nmr spectrum of the corresponding methyl ester of 6 was as follows: ($CDCl_3$) : δ 3.05 (t, 2H, $\underline{CH_2}CO_2CH_3$), 3.55 (t, 2H, $\underline{CH_2}CO$), 4.0 (s, 3H, $CO_2\underline{CH_3}$), 7.8-8.2 (m, 6H, H_{4-9}), 8.3 (s, 1H, H_3); MS (m/e) : 308 (M^+), 263 (M-45, CO_2H), 235 (M-73, $CH_2CH_2CO_2H$), 221, 207 (235-CO, 163 (207-CS).

γ-(2-Acenaphtho[1,2-b]thienyl)butyric acid (7).- A mixture of the ketoacid 6 (0.5 g, 1.6 mmol), hydrazine hydrate 90% (1 ml), KOH (0.5 g, 8.9 mmol) and diethyleneglycol (6-8 ml) was refluxed for 4 hrs. Then part of hydrazine hydrated was removed by distillation till the temperature reached 180°-190°. The residue was then refluxed for 3 hrs, cooled, diluted with water (50-60 ml) and acidified with conc. HCl. The solid which separated was collected, washed well with water and dried, recrystallization from carbon tetrchloride afforded 7 as a yellowish brown solid (0.43 g, 90%), mp. 135-136°. IR (Nujol) : 1675 (CO_2H), 3180 (OH) cm^{-1}; nmr ($CDCl_3$) : δ 1.90-2.25 (m, 2H, $\underline{CH_2}CH_2CO_2H$), 2.47 (t, 2H, $\underline{CH_2}Ar$), 3.02 (t, 2H, $\underline{CH_2}CH_2CO_2H$), 7.2-7.9 (m 7H, aromatic).

Anal. Calcd. for $C_{18}H_{14}O_2S$: C, 73.47; H, 4.76

Found : C, 73.22; H, 4.52

The nmr spectrum of the corresponding methyl ester of 7 ($CDCl_3$) : δ 1.82 (m, 2H, $\underline{CH_2}CH_2CO_2CH_3$), 2.20 (t, 2H, $\underline{CH_2}Ar$), 2.8 (t, 2H, $\underline{CH_2}CO_2CH_3$), 3.5 (s, 3H, $CO_2\underline{CH_3}$), 7.0-7.7 (m, 7H, aromatic); MS (m/e) : 294 (M^+), 221 (M-73, $CH_2CH_2CO_2H$).

Acenaphtho[1,2-b]-11-oxo-8,9,10,11-tetrahydrobenzo[d]thiophene (9).- A 0.3 g (1 mmol) sample of the acid 7 was refluxed with PCl_5 (0.2 g, 1 mmol) in 20 ml of dry CCl_4 for 3 hrs. Removal of solvent *in vacuo* afforded the acid chloride 8 as a yellowish brown viscous oil. The crude acid chloride was immediately dissolved in 24-30 ml of dry CS_2 and 0.5 ml of anhydrous $SnCl_4$ was added. The mixture was stirred at room temperature for 30 min. followed by reflux for 2.5 hrs. After decomposing the complex by ice-water, the organic material was extrcted into 50 ml CH_2Cl_2, washed with water, dried (Na_2SO_4). Removal of solvent gave a brownish yellow solid which was purified by passing through a column of silica gel and eluted with benzene. Removal of solvent furnished 225 mg (80%) of 9 as yellow solid, mp. 153-154° (ether). IR ($CHCl_3$) : 1670 (C=O) cm^{-1}; nmr ($CDCl_3$) : δ 2.05-2.30 (m, 2H, $\underline{CH_2}$), 2.60 (t, 2H, $CO\underline{CH_2}$), 3.05 (t, 2H, $\underline{CH_2}Ar$), 7.45-7.90 (m, 5H, H_{2-6}), 8.67 (d, 1H, H_1); MS (m/e) : 276 (M^+), 220 (M-56, CH_2CH_2CO), 176.

Anal. Calcd. for $C_{18}H_{12}OS$: C, 78.26; H, 4.35

Found : C, 78.12; H, 4.26

Acenaphtho[1,2-b]-11-hydroxy-8,9,10,11-tetrahydrobenzo[d]thi-

ophene (10).- To a solution of ketone 9 (100 mg, 0.36 mmol) in 5 ml THF and 2 ml methanol, was added $NaBH_4$ (120 mg) portion-wise, and the mixture was stirred at rt for 12 hrs. The solvent was removed in vacuo, and the residue was diluted with water and extracted with dichloromethane. After the usual work-up, 100 mg (99%) of the alcohol 10 was obtained as yellow solid, mp. 141° (ether-pet ether). IR ($CHCl_3$) : 3570 (-OH) cm^{-1}; nmr ($CDCl_3$) : δ 1.7-2.0 (m, 5H, CH_2 and CH), 2.7-2.9 (m, 2H, CH_2Ar), 4.9-5.2 (br, s, 1H, OH), 7.4-8.0 (m, 6H, aromatic).

Anal. Calcd. for $C_{18}H_{14}OS$:C, 77.70; H, 5.04
Found : C, 77.62; H, 5.01

Acenaphtho[1,2-b]-8,9-dihydrobenzo[d]thiophene (11).- The alcohol 10 (230 mg, 0.83 mmol) in 100 ml dry benzene was refluxed with p-toluenesulfonic acid (10 mg) for 1 hr., cooled and washed with water. The benzene layer was dried (Na_2SO_4) and solvent was removed at reduced pressure.The residue obtained was purified by chromatography (silica gel, hexane) and yielded 175 mg (81%) of 11, mp. 102-103°. IR ($CHCl_3$) : 1600 (C=C) cm^{-1}; nmr ($CDCl_3$) : δ 1.2-3.0 (br, m, 4H, $2CH_2$), 5.6-6.0 (m, 1H, vinylic H_{10}), 6.5-6.8 (m, 1H, vinylic H_{11}), 7.0-8.2 (m, 6H, aromatic).

Anal. Calcd. for $C_{18}H_{12}S$:C,83.08;H, 4.62
Found : C, 82.95; H, 4.50

Acenaphtho[1,2-b]-8,9,10,11-tetrahydrobenzo[d]thiophene (12).- A mixture of 100 mg (0.36 mmol) of ketone 9, trifluoroacetic acid (5 ml), triethylsilane (4 ml) was stirred at room

temperature for 3 hrs. It was then poured in water and extracted with ether; the ethereal layer was washed with water, dried (Na_2SO_4) and the solvent was removed.The crude product obtained on passing through a column of silica gel using hexane as eluent afforded 80 mg (84%) of 12 as an off-white solid, mp. 96-97°.

Anal. Calcd. for $C_{18}H_{14}S$: C, 82.44; H, 5.34

Found : C, 82.19; H, 5.28

Acenaphtho[1,2-b]benzo[d]thiophene (13).- A 50 mg (0.19 mmol) sample of 11 was refluxed under N_2 with 100 mg (0.44 mmol) of DDQ in 20 ml dry benzene overnight. The mixture was then filtered through a column of florisil. Removal of solvent afforded 13 as a yellow solid was further purified by column chromatography (neutral alumina, 4:1 pet. ether-benzene) to yield 45 mg (90%) of 13 as a colorless solid, mp. 124-125°. nmr ($CDCl_3$) : δ 7.1-8.0 (m, 10H, aromatic); MS (m/e) : 260 (M+2)), 259 (M+1), 258 (M^+), 129.

Anal. Calcd. for $C_{18}H_{10}S$: C, 83.72; H, 3.88

Found : C, 83.49; H, 3.69

Acenaphtho[1,2-b]benzo[d]thiophene (13).- A 40 mg (0.15 mmol) sample of 12 was aromatized with 200 mg of DDQ in 25 ml benzene as described above and gave the desired product 13 in quantitative yield, mp. and mixed mp. 125°.

Acknowledgement.- We thank Dr. J.R. Grezes, Freiburg, West Germany and Dr. P. N. Moza, Freising, West Germany, for some MS and NMR spectra. We are thankful to C.S.I.R., New Delhi, for financial assistance.

REFERENCES

† Previous paper in this series : D.Ramesh, B.G. Chatterjee and J.K. Ray, Ind. J. Chem., 25B, 964 (1986).

1. C.W. Thornber, Chem.Soc. Rev., 8, 563 (1979).
2. M.L. Lee, C.Willey, R.N. Castle and C. White, "Polynuclear Aromatic Hydrocarbons Chemistry and Biological Effects", A. Bjorseth and A. Dennis,Eds, Battelle,Columbus, p. 59 (1980).
3. C. Willey, M. Iwao, R.N. Castle and M.L. Lee, Anal. Chem., 53, 400 (1981); N.P. Buu-Hoi, Quart. Rep. Sulfur Chem., 5, 9 (1970).
4. R.A. Pelroy, D.L. Stewart, Y. Tominaga, M. Iwao, R.N. Castle and M.L. Lee, Mutat, Res., 117, 31 (1983).
5. M.L. Tedjamulia, Y.Tominaga,R.N.Castle and M.L. Lee, J. Heterocyclic Chem., 20, 861 (1983).
6. V. Hauptmann, M. Scholz,.H. Koehler and H. Hofmann, J. prakt. Chem., 311, 614 (1969).
7. J.K. Ray, G.K. Kar and B.G. Chatterjee, Tetrahedron, 40, 2959 (1984).
8. M. Ghosh, R. Mukherjee, B.G. Chatterjee and J.K. Ray, Ind. J. Chem., 20B, 243 (1981) and reference 3 of that paper.
9. L.J. Durham, D.J. McLeod and J. Cason, Org. Syn., Col. Vol. 4, 510 (1963).
10. J.S. Swenton and P.W. Raynolds, J. Am.Chem. Soc., 100, 6188 (1978).

(Received May 12, 1987; in revised form August 31, 1987)