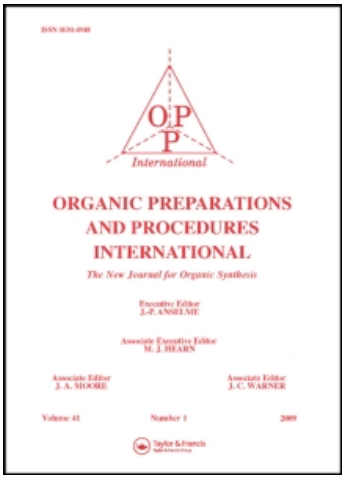



**Organic Preparations and Procedures International**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

# AN IMPROVED SYNTHESIS OF THIENO(2,3-B)QUINOLINES *via* S-OXIDES

S. P. Rajendran[a]; P. Shanmugam[a]
[a] Department of Chemistry, Bharathiar University, Coimbatore, INDIA

**To cite this Article** Rajendran, S. P. and Shanmugam, P.(1994) 'AN IMPROVED SYNTHESIS OF THIENO(2,3-B)QUINOLINES *via* S-OXIDES', Organic Preparations and Procedures International, 26: 3, 349 — 352
**To link to this Article: DOI:** 10.1080/00304949409458434
**URL:** http://dx.doi.org/10.1080/00304949409458434

3. R. R. Gupta, K .G. Ojha and M. Kumar, *J. Heterocycl. Chem.*, **17**, 1325 (1980); R .L. Dannley and D .A. Zazaris, Can. J. Chem., **43**, 2610 (1965); R. L. Mital and S. .K. Jain, *J. Chem. Soc. (C)*, 2148 (**1969**); K .J. Farrington and W. K. Warburton, *Aust. J. Chem.*, **8**, 545 (1955).

********

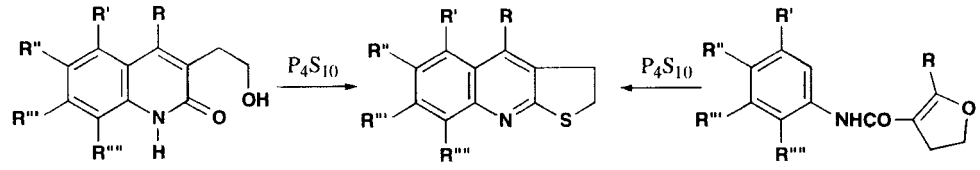
## AN IMPROVED SYNTHESIS OF THIENO(2,3-b)QUINOLINES *via* S-OXIDES

*Submitted by* S. P. Rajendran* and P. Shanmugam
(02/03/93)

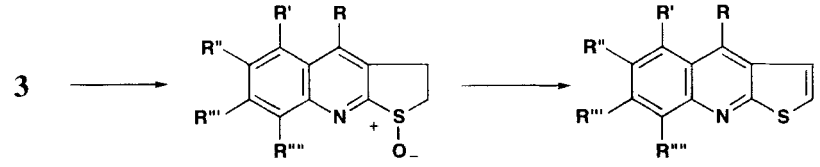
*Department of Chemistry*
*Bharathiar University*
*Coimbatore - 641 046, INDIA*



Earlier, we reported two convenient methods for the preparation of 2,3dihydrothieno(2,3-b)quinoline (**3**) and its derivatives.[1,2] These involved heating 3-(2'-hydroxyethyl)quinolin-2(1H)-one (**1**) or 4,5-dihydrofuran-3-carboxanilide (**2**) with tetraphosphorus decasulfide.[1] Of these two procedures, the former based on the use of quinolonyl ethanols (**1**) is quite useful, particularly since a variety of quinolonyl ethanols are available.[3,4] Kuwayama[5] prepared the parent thienoquinoline **5a** *via*




**1** **3** **2**




**4** **5**

a) R = R' = R" = R"' = R"" = H b) R = R' = R"' = R"" = H, R" = $CH_3$
c) R = R" = R"' = H, R' = R"" = $OCH_3$ d) R = R" = R"' = H, R' = R"" = $CH_3$
e) R = R" = R"' = H, R' = Cl, R"" = $OCH_3$ f) R = R' = R" = H, R"' = R"" = CH=CH–CH=CH
g) R = $CH_3$, R' = R" = R"' = R"" = H h) R = $C_6H_5$, R' = R" = R"' = R"" = H
i) R = $C_6H_4$(*p*-$CH_3$), R' = R" = R"' = R"" = H

S-oxidation of **3a** with perphthalic acid and refluxing the S-oxide with acetic anhydride.[5] However in the perpthalic acid oxidation, the yield of S-oxide was only 46% and the product was contaminated with S,S-dioxide, S,S,N-trioxide and N-oxide. It was felt that a clean conversion of **3a** to its S-oxide

would enhance the overall yield of thienoquinolines. We now report that $NaIO_4$ in ethanol,[6,7] improves the yield of S-oxide to about 89%.

When compound **3a** was stirred with one equivalent of $NaIO_4$ in ethanol/water at 0°, a colorless product was isolated in 82% yield and was identified as the S-oxide **4a** (mp., NMR, IR, mass spectrum). When the experiment was repeated with a two-fold excess or more of the oxidant, only the S-oxide **4a** was formed (85-89% yield). Then the conversion of **4a** to **5a** was effected by $Ac_2O$ in 88% yield according to the procedure of Kuwayama.[5] Therefore, the overall 78% yield for the transformation of **3a** to **5a** *via* S-oxide **4a** is better than the previously reported 67% conversion by the sequence of allylic bromination with NBS and dehydrobromination with DBU.[2] This improved technique was then extended to various derivatives (Tables 1 and 2).

**TABLE 1**. 2,3-Dihydrothieno(2,3-b)quinoline-1-oxides (**4**) from **3**

| Cmpd | Yield (%) | mp. (°C) | Elemental Analysis (Found) C | H | N | IR[d] ($cm^{-1}$) |
|---|---|---|---|---|---|---|
| **4a** | 89 | 144-145[a,b] | 64.99 (64.83) | 4.46 (4.32) | 6.89 (6.71) | 3000,1025 (S=O) |
| **4b** | 80 | 211-213[c] | 66.33 (66.21) | 5.10 (4.99) | 6.45 (6.32) | 3000,1030 (S=O) |
| **4c** | 52 | 223-224[b] | 59.30 (59.13) | 4.98 (4.87) | 5.32 (5.41) | 3000,1040 (S=O) |
| **4d** | 34 | 205-207[b] | 67.50 (67.28) | 5.67 (5.52) | 6.06 (6.12) | 3000, 1045 (S=O) |
| **4e** | 46 | 202-203[b] | 53.83 (53.62) | 3.77 (3.71) | 5.23 (5.11) | 3000,1045 (S=O) |
| **4f** | 69 | 204-206[b] | 71.12 (70.99) | 4.38 (4.24) | 5.53 (5. 39) | 3020,1035 (S=O) |
| **4g** | 72 | 215-217[c] | 66.33 (66.25) | 5.10 (5.21) | 6.45 (6.37) | 3000,1035[e] (S=O) |
| **4h** | 76 | 185-187[c] | 73.09 (72.91) | 4.69 (4.52) | 5.01 (5.12) | 3000,1045[e] (S=O) |
| **4i** | 69 | 228-230[c] | 73.69 (73.59) | 5.15 (5.23) | 4.77 (4.68) | 3010,1040[e] (S=O) |

a) Lit.[5] mp. 144-146° b) From $CHCl_3$ c) From $CHCl_3$-MeOH d) in $CHCl_3$ unless otherwise specified e) As KBr pellet

$^1H$ NMR ($CDCl_3$-DMSO-$d_6$): **Compound 4a**: δ 3.23-3.9 (m, 4H, $SOCH_2CH_2$-), 7.6-8.16 (m, 4H, Ar-H), 8.5 (s, 1H, $C_4$-H). **Compound 4f**: δ 3.23-3.9 (m, 4H, SO-$CH_2CH_2$), 7.76-8.14 (m, 5H, ArH), 8.51 (s, 1H, $C_4$-H), 9.2 (m, 1H, $C_9$-H). **Compound 4h**: δ 3.2-3.4 (m, 4H, -$CH_2$-$CH_2$), 7.33-7.9 (m, 9H, ArH).

It is pertinent to mention that combination of the present methodology with the previously reported photolytic technique for the preparation of parent quinolone alcohols (**1**)[4] from N-phenyl-4,5-dihydrofuran-3-carboxanilides (**2**), provides a more reliable sequence for the preparation of 4H-deri-

vatives of thieno(2,3-b)quinolines (**5**). The conversion of **2a** using this improved synthetic sequence results in a overall yield of **5a** in 48%.

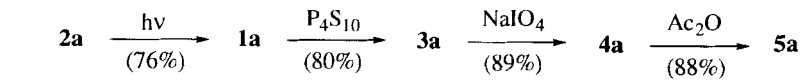



**TABLE 2.** Yield of Thieno(2,3-b)quinolines (**5**) from **4**

| Cmpd | Yield (%) | mp.(°C)[a] (lit.) | Elemental Analysis (Found) C | H | N | IR ($cm^{-1}$) ($CHCl_3$) |
|---|---|---|---|---|---|---|
| **5a** | 88 | 107-108 (107-108)[8] | 71.32 (71.50) | 3.80 (3.89) | 7.56 (7.49) | 1610, 1590, 1559, 1330, 1200 |
| **5b** | 79 | 131-132 (131-132)[8] | 72.31 (72.5) | 4.56 (4.52) | 7.03 (7.20) | 1615, 1570 1490, 1440, 1300, 1200 |
| **5g** | 72 | 90-91 (91-92)[9] | 72.31 (72.41) | 4.56 (4.59) | 7.03 (7.11) | 1610, 1580, 1550, 1480 1390 |
| **5h** | 88 | 118-119[b] (119-120)[9] | 78.13 (78.30) | 4.24 (4.45) | 5.36 (5.30) | 1620, 1555, 1485, 1380 |

a) From petroleum-ether unless noted otherwise b) From benzene-pet ether.

$^1$H NMR ($CDCl_3$): **Compound 5a**: δ 7.62 (d, 1H, J = 6Hz, $C_2$-H), 7.32 (d, 1H, J = 6Hz, $C_3$H), 8.52 (s,1H, $C_4$-H), 7.62-7.85 (m, 2H, $C_6$-H, $C_7$-H), 7.88 (dd, 1H, $C_5$-H, J = 8, 1.5Hz), 8.27 (dd, 1H, $C_8$-H, J = 8, 1.5Hz). **Compound 5b**: δ 7. 53 (d, 1H, J= 6Hz, $C_2$-H), 7.33 (d, 1H, J = 6Hz,$C_3$H), 8.43 (s, 1H, $C_4$-H), 7.57-7.80 (m ,2H, $C_5$-H and $C_7$-H), 8.07 (d, 1H, J = 8Hz, $C_8$-H), 2.57 (s, 3H, $CH_3$).

**Compound 5g:** δ 2.85 (s, 3H, $C_4$-$CH_3$), 7.28-8.33 (m, 6H, ArH)

**Compound 5h:** δ 7.08 (d, 1H, J = 6Hz, $C_2$H), 7.21-8.33 (m, 10H, $C_3$-H, other ArH)

## EXPERIMENTAL SECTION

Melting points were taken on Boetius heating table and are uncorrected. IR Spectra were recorded on a Beckmann IR 20 and Perkin Elmer Model 597 Spectrophotometer, PMR spectra on a Varian T-60 and EM-390 spectrometers using TMS as internal reference and mass spectra on a Hitachi Perkin-Elmer -RMU-6E instrument at 70 eV.

**2,3-dihydrothieno(2,3-b)quinoline (3).- 3a-3i**[1,8,9] are all known and were prepared by heating **1a-1i**[3,4,10,11] with $P_4S_{10}$.[1]

**2,3-Dihydrothieno(2,3-b)quinoline-1-oxides (4a-4i).**- A solution of **3** (1 m. mole) in 50 mL of ethanol was stirred with a solution of sodium metaperiodate (2.1 mmol) in an ice-cold (0°C) bath. The mixture was stirred for 4-8 hrs. After the formation of thick white precipitate, the reaction mixture was diluted with water and extracted with chloroform. The extract was dried and evaporated . The residue

was purified by column chromatography over silica (60-120 mesh); the product was eluted with chloroform-ethyl acetate (2:1) and was then recrystallized (Table 1).

**Thieno(2,3-b)quinoline (5a-5b; 5g-5h).**- A mixture of 4 (100 mg) and freshly distilled acetic anhydride (1 mL) was refluxed for 2-3 hrs. Excess acetic anhydride was removed under reduced pressure and the residue was poured into ice-water. The solution was neutralized with 10% NaOH and extracted with chloroform. The dried solution was evaporated in vacuo and the residue obtained was chromatographed over a column of basic alumina using benzene-petrol as eluent. The product was then recrystallized from a suitable solvent (Table 2).

**Acknowledgement**.- The authors are thankful to Dr. S. Rajappa, CIBA-Geigy Research Centre, Bombay and Dr. R. Hull, Imperial Chemical Industries Ltd., Alderley Park, Cheshire, England for the mass and NMR spectra.

## REFERENCES

1. P. Shanmugam, T. K. Thiruvengadam, and N. Soundararajan, *Org. Prep. Proced. Int.*, **8**, 279 (1976).

2. A. Gnanasekaran, N. Soundararajan and P. Shanmugam, *Synthesis*, 612 (**1977**).

3. P. Shanmugam, T. K. Thiruvengadam and R. Palaniappan, *Z. Naturforsch*, **28b**, 551 (1973); P. Shanmugam, T. K. Thiruvengadam and K. Ramasgamy, *Monatsh. Chem.*, **108**, 725 (1975); T. K. Thiruvengadam, Ph. D. Thesis, University of Madras, India, pp. 162-170 (1976).

4. S. P. Rajendran, V. Ariswaran, M. Ramesh and P. Shanmugam, *Synthesis*, 160 (**1982**).

5. a) Y. Kuwayama, *Yakugaku Zasshi*, **81**, 1278, 1501 (1961): *C.A.*, **57**, 13743, 13744 (1962); b) G. Kobayashi, Y. Kuwayama and S. Okamura, *Yakugaku Zasshi*, **83**, 235(1963): *C.A.*, **59**, 5144 (1963).

6. N. J. Leonard and C. R. Johnson, *J. Org. Chem.*, **27**, 282 (1962).

7. C. R. Johnson and D. McCants Jr., *J. Am. Chem. Soc.*, **87**, 1109 (1965).

8. A. Gnanasekaran, Ph. D. Thesis, University of Madras, India, pp. 88-120 (1979)

9. P. Shanmugam, K. Kanakarajan, N. Soundararajan and A. Gnanasekaran, *Synthesis*, 253 (**1976**)

10. K. Ramasgamy, Ph. D. Thesis, University of Madras, India, pp.119-121 (1978).

11. K. Paramasivam, K. Ramasgamy and P. Shanmugam, *Synthesis*, 768 (**1977**).

********