A Convenient Synthesis of Azuleno[2,1-*b*]thiophene

Kameji YAMANE,* Kunihide FUJIMORI,* and Toru TAKEUCHI
Department of Chemistry, Faculty of Science, Shinshu University, Asahi, Matsumoto 390
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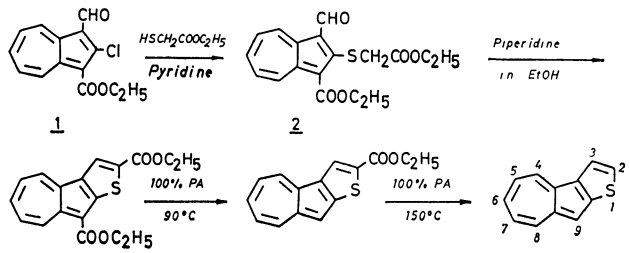
Synopsis. Azuleno[2,1-*b*]thiophene and its derivatives were prepared from ethyl 2-chloro-3-formylazulene-1-carboxylate and ethyl mercaptoacetate in a few steps.

Azuleno[2,1-*b*]thiophene, which is a polycyclic aromatic compound containing a heterocycle, is of interest in its physical properties and chemical behavior. The compound and related compounds have so far been prepared by reaction of diethyl 2-chloroazulene-1,3-dicarboxylate with ethyl mercaptoacetate, followed by cyclization, methylation, hydrolysis, decarboxylation, reduction, and dehydration.[1)]

We now wish to report a convenient synthesis of the title compound and its derivatives.

When ethyl 2-ethoxycarbonylmethylthio-3-formylazulene-1-carboxylate (**2**) prepared by the reaction of ethyl 2-chloro-3-formylazulene-1-carboxylate (**1**)[2)] with ethyl mercaptoacetate was heated with piperidine in EtOH, cyclization occurred to afford the diethyl azuleno[2,1-*b*]thiophene-2,9-dicarboxylate (**3**) in good yield. The conversion of **2** to **3** could also be carried out with basic activated alumina. The compound **3**, on treatment with 100% phosphoric acid at 90 °C, gave ethyl azuleno[2,1-*b*]thiophene-2-carboxylate (**4**). When the ester (**4**) was heated at 150 °C in 100% phosphoric acid, deethoxycarbonylation occurred to give azuleno[2,1-*b*]thiophene (**5**). The compound **5** was also obtained from **4** as follows. Compound **4** was hydrolyzed in ethanolic KOH and the resulting carboxylic acid was heated at 170—180 °C under reduced pressure (2 mmHg†) to yield **5**.



1 2 3 4 5

The spectral data of **2**, **3**, **4**, and **5** are shown in the experimental section.

The NMR vicinal coupling constants indicate that 7-membered rings of **3**, **4**, and **5** exhibit some bond length alternation, similar to the results for benz[*a*]azulene;[3)] this behavior is characteristic of polyenes. (Table 1).

TABLE 1. NMR VICINAL COUPLING CONSTANTS OF **3**, **4**, AND **5**

Compound	J_{45}/Hz	J_{78}/Hz	ΔJ/Hz
3	9.0	10.2	1.2
4	9.0	10.2	1.2
5	8.5	10.0	1.5

† 1 mmHg=133.322 Pa.

Experimental

All melting points are uncorrected.

Ethyl 2-Ethoxy Carbonylmethylthio-3-formylazulene-1-carboxylate (**2**). A mixture of ethyl 2-chloro-3-formylazulene-1-carboxylate (51.8 mg), ethyl mercaptoacetate (60 mg), and pyridine (3 ml) was heated at 100 °C on an oil bath for 15 min. After cooling, the reaction mixture was poured into water, acidified with 2 mol dm^{-1} sulfuric acid, and extracted with chloroform. The chloroform layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The residue was chromatographed on a silica-gel column with benzene–chloroform (1 : 1). The red effluent was freed from solvent to give **2** (52.4 mg, 76.7%) as red oil, which was used for the next step without further purification.

^{1}H NMR ($CDCl_3$) δ ppm: 1.09 (3H, t, J=7.5 Hz, $SCH_2COOCH_2C\underline{H}_3$), 1.50 (3H, t, J=7.5 Hz, $COOCH_2C\underline{H}_3$), 3.37 (2H, s, $SC\underline{H}_2COOCH_2CH_3$), 4.02 (2H, q, J=7.5 Hz, $SCH_2COOC\underline{H}_2CH_3$), 4.51 (2H, q, J=7.5 Hz, $COOC\underline{H}_2CH_3$), 7.8—8.0 (3H, m, H-5,6,7), 9.4—9.7 (1H, m, H-8 or H-4), 9.8—10.0 (1H, m, H-4 or H-8).

IR ($CDCl_3$): 2992, 1734, 1696, 1652, 1441, 1403, 1195, 647 cm^{-1}.

*Diethyl Azuleno[2,1-*b*]thiophene-2,9-dicarboxylate* (**3**). *a*): Three drops of piperidine were added to a solution of **2** (177.3 mg) in ethanol (17 ml). The mixture was refluxed for 1 h. The reaction mixture was freed from solvent and the residue was chromatographed on a silica-gel column with chloroform. The yellowish brown effluent was evaporated under reduced pressure. The residue was recrystallized from cyclohexane to give **4** (155.6 mg, 92.6%) as yellowish brown needles; mp 136—137 °C.

IR (KBr): 2989, 1695, 1249, 779, 727 cm^{-1}.

ES λ_{max} in cyclohexane ,nm (log ε): 215 (4.27), 252 (4.31), 321 (4.74), 337 (4.80), 348 (4.08), 386 (3.62), 402 (3.80), 409 (3.70), 428 (4.01), 574 (2.45).

^{1}H NMR ($CDCl_3$) δ ppm: 1.44 (3H, t, J=7.0 Hz, 2-$COOCH_2C\underline{H}_3$), 1.51 (3H, t, J=7.0 Hz, 9-$COOCH_2C\underline{H}_3$), 4.40 (2H, q, J=7.0 Hz, 2-$COOC\underline{H}_2CH_3$), 4.43 (2H, q, J=7.0 Hz, 9-$COOC\underline{H}_2CH_3$), 7.2—7.9 (3H, m, H-5,6,7), 8.19 (1H, s, H-3), 8.39 (1H, d, J=9.0 Hz, H-4), 9.43 (1H, d, J=10.2 Hz, H-8).

^{13}C NMR ($CDCl_3$) δ ppm: 14.5 (q), 14.6 (q), 60.3 (t), 61.2 (t), 109.3 (s), 124.6 (d), 128.4 (d), 129.5 (d), 133.6 (d), 133.9 (s), 134.0 (s), 136.4 (d), 137.0 (s), 138.1 (d), 145.2 (s), 153.9 (s), 163.2 (s), 164.1 (s).

Found: C, 65.92; H, 4.85; S, 10.02%. Calcd for $C_{18}H_{16}O_4S$: C, 65.84; H, 4.91; S, 9.76%.

b): Compound **2** (29.9 mg) was dissolved in chloroform and adsorbed on a basic alumina column. After standing overnight, the reaction mixture was eluted with chloroform. From the yellowish brown effluent, **3** was obtained as yellowish brown needles (16 mg, 56.4%); mp 136—137 °C. The IR spectrum was identical with that of a sample prepared by Method *a*) and the mixed melting point was not depressed.

*Ethyl Azuleno[2,1-*b*]thiophene-2-carboxylate* (**4**). A mixture of bis (ethoxycarbonyl) compound (**3**) (121.4 mg) and 100% phosphoric acid (5 ml) was heated at 90 °C for 1 h. After cooling, the reaction mixture was poured into water and extracted with chloroform. The extract was dried, freed

from solvent, and the residue was chromatographed on silica gel. Elution with benzene gave bluish green plates (90 mg, 94.4%); mp 86.5—87.5 °C, which were recrystallized from cyclohexane.

IR (KBr): 2985, 1695, 1510, 1253, 1243, 719 cm^{-1}.

ES λ max in cyclohexane nm (log ε): 216 (4.06), 236 (4.21), 319 (4.82), 332 (4.98), 358 (3.86), 363 (3.56), 376 (3.83), 396 (4.01), 407 (3.65), 420 (4.04), 599 (2.88).

^{1}H NMR ($CDCl_3$) δ ppm: 1.43 (3H, t, J=7.0 Hz, $COOCH_2\underline{CH_3}$), 4.40 (2H, q, J=7.0 Hz, $COO\underline{CH_2}CH_3$), 7.0—7.7 (4H, m, H-5,6,7,9), 8.14 (1H, d, J=10.2 Hz, H-8), 8.33 (1H, dm, J=9.0 Hz, H-4), 8.39 (1H, s, H-3).

^{13}C NMR ($CDCl_3$) δ ppm: 14.5 (q), 61.1 (t), 109.9 (d), 124.5 (d), 125.0 (d), 125.3 (d), 131.5 (d), 132.4 (s), 134.7 (s), 135.8 (d), 135.8 (s), 136.3 (d), 143.8 (s), 152.5 (s), 163.4 (s).

Found: C, 70.25; H, 4.79; S, 12.56%. Calcd for $C_{15}H_{12}O_2S$: C, 70.29; H, 4.72; S, 12.51%.

Azuleno[2,1-b]thiophene (5). *a)*: A mixture of **4** (25 mg) and 100% phosphoric acid was heated at 150 °C for 2 h. After cooling, the reaction mixture was diluted with water and extracted with chloroform. The extract was dried, evaporated under reduced pressure, and the residue was chromatographed on alumina column. From benzene effluent, **5** was obtained as bluish green plates (12 mg, 66.8%); mp 173—174 °C, which were recrystallized from ethanol. The UV spectrum was identical with that of azuleno[2,1-*b*]-thiophene prepared by Matsui *et al.*[1]

^{1}H NMR ($CDCl_3$) δ ppm: 6.9—7.6 (3H, m, H-5,6,7), 7.47 (1H, s, H-9), 7.32 (1H, d, J=5.4 Hz, H-3), 7.69 (1H, d, J=5.4 Hz, H-2), 8.20 (1H, d, J=10.0 Hz, H-8), 8.39 (1H, d, J=8.5 Hz, H-4).

^{13}C NMR ($CDCl_3$) δ ppm: 109.4 (d), 118.6 (d), 122.5 (d), 123.4 (d), 125.5 (d), 131.1 (d), 132.5 (s), 135.7 (d), 136.9 (s), 141.7 (s), 149.7 (s).

b): A mixture of **4** (202 mg), ethanol, and 20% potassium hydroxide aqueous solution was refluxed for 30 min. After removal of the solvent, water was added to the residue. When the solution was made acid with 2 mol dm^{-3} sulfuric acid, a green precipitate separated out. The precipitate was filtered off, washed with a small amount of ethanol to give azuleno-[2,1-*b*]thiophene-2-carboxylic acid as green powder (173 mg, 96.5%); this was used for the next step without further purification.

The carboxylic acid obtained above was heated under reduced pressure (2 mmHg) in a sublimation aparatus. The bluish green crystals was sublimed at 170—180 °C. Recrystallization from ethanol gave bluish green plates (18 mg, 46.1%); mp 173—174 °C. The IR spectrum was identical with that of the sample obtained by Method *a)*, and the mixed melting point was not depressed.

References

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