

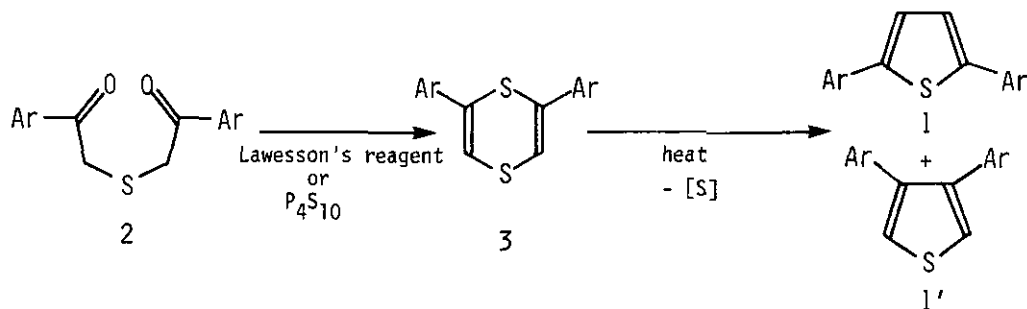
PREPARATION OF NATURALLY OCCURRING α -TERTHIOPHENES
(2,2':5',2''-TERTHIOPHENES)

Juzo Nakayama,* Yoichi Nakamura, Takayuki Tajiri,
and Masamatsu Hoshino
Department of Chemistry, Faculty of Science, Saitama University,
Urawa, Saitama 338, Japan

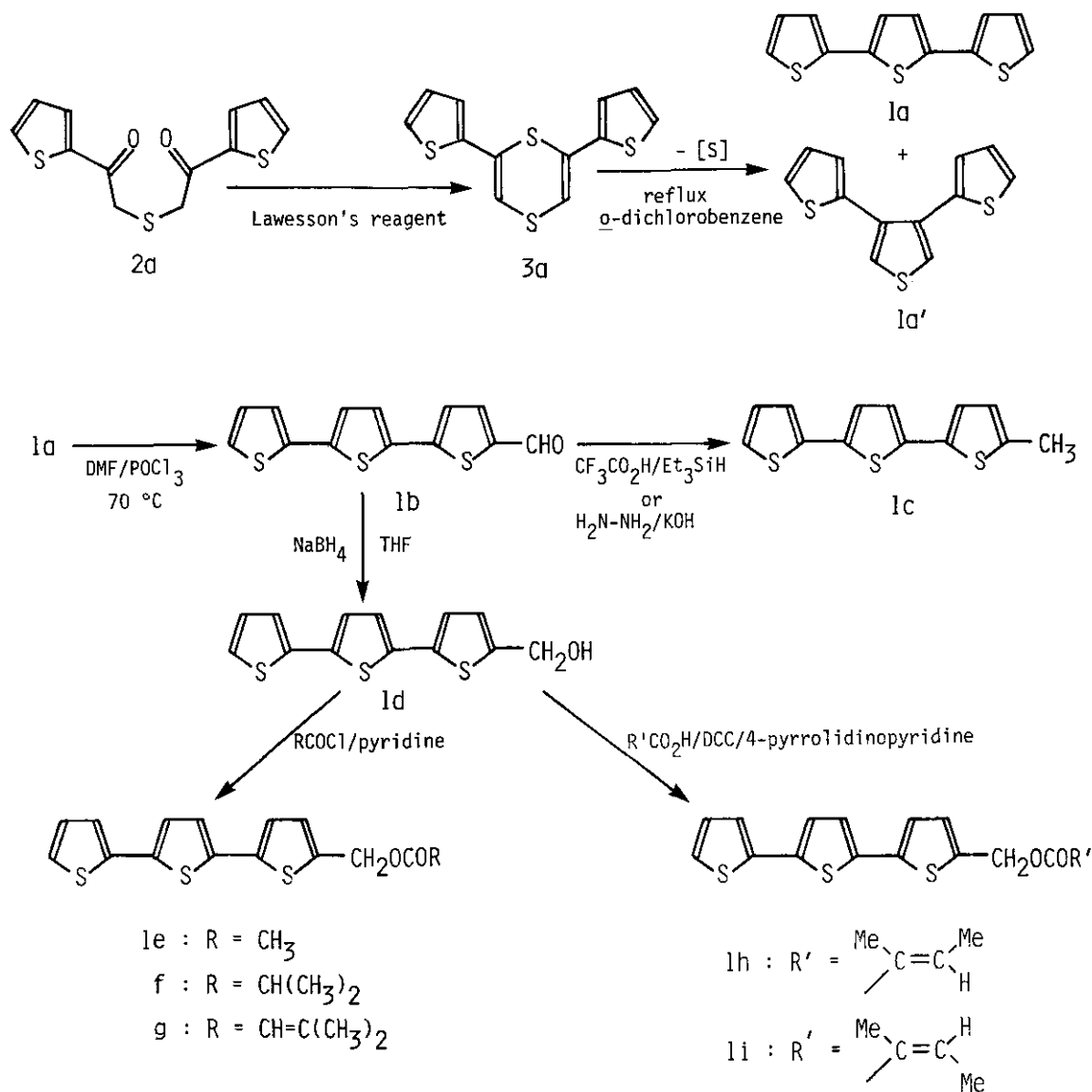
Abstract — A series of naturally occurring α -terthiophenes (2,2':5',2''-terthiophenes) were prepared using readily accessible bis[2-oxo-2-(2-thienyl)ethyl] sulfide as the starting material.

Biological properties of α -terthiophene (2,2':5',2''-terthiophene) (1a) and its derivatives have attracted much attention.¹ Terthiophene 1a was first obtained as a byproduct in the preparation of 2,2'-bithiophene² and later characterized in the petals of the yellow marigold (*Tagetes erecta*).³ Other plants belonging to the family *Compositae* also contain 1a and its derivatives.⁴ Especially a series of terthiophene derivatives (1a-i) were isolated from *Eclipta erecta* L.^{4a} It also contains polyacetylenes and thiophene and 2,2'-bithiophene derivatives related to 1a-i. Herein we report the preparation of these naturally occurring terthiophenes using readily accessible bis[2-oxo-2-(2-thienyl)ethyl] sulfide as the starting material.

We recently reported a facile preparation of 2,6-diaryl-1,4-dithiins (3) from diketo sulfides (2) by treatment with P_4S_{10} or Lawesson's reagent.⁵ Heating 3 in boiling *o*-dichlorobenzene affords, with loss of sulfur, isomeric mixtures of



2,5- and 3,4-diarylthiophenes (1 and 1') in good yields, thereby the former isomer being predominantly formed.⁶ Application of this reaction sequence to bis[2-oxo-2-(2-thienyl)ethyl] sulfide (2a)⁷ enables to prepare 1a in a large quantity. Heating 2a (0.5 mol) with Lawesson's reagent (0.6 mol) in boiling benzene (750 ml) for 2 h affords 2,6-di(2-thienyl)-1,4-dithiin (3a) in 65-70% yield. Heating 3a (0.2 mol) in boiling *o*-dichlorobenzene (500 ml) for 1 h gives an isomeric mixture of 1a and 1a' in a ratio of 13:1. Chromatographic purification followed by recrystallization from hexane affords pure 1a, mp 96-97 °C (lit.,² mp 93-94 °C), in 35% yield.^{8,9}



The Vilsmeier reaction of 1a (20 mmol) with phosphorus oxychloride (21 mmol) and *N,N*-dimethylformamide (40 ml) at 70 °C for 1 h afforded the aldehyde 1b, mp 140-141 °C (from benzene) (lit.,^{4a} mp 135-136 °C), in 75% yield with 18% recovery of 1a. ¹HNMR, IR, and UV data of 1b thus obtained agreed with those of 1b from *Eclipta erecta*.^{4a}

The reduction of 1b with triethylsilane and trifluoroacetic acid¹⁰ in refluxing chloroform furnished the methyl derivative 1c,¹¹ mp 98-99 °C (from MeOH) (lit.,¹² mp 93-94.5 °C), in 20% yield. More satisfactory result was obtained by Wolff-Kishner reduction; heating 1b, hydrazine hydrate, and potassium hydroxide in boiling diethylene glycol for 0.5 h gave rise to 1c in 96% yield.

The reduction of 1b with sodium borohydride in THF at room temperature afforded the alcohol 1d, mp 151-152 °C (from chloroform) (lit.,^{4d} mp 150.5-151 °C), quantitatively. Spectroscopic data of 1d are consistent with those of 1d isolated from *Eclipta alba*.^{4d}

The acetate 1e, mp 113-114 °C (from hexane) (lit.,^{4a} mp 114-115 °C), was obtained quantitatively by treatment of 1d with acetyl chloride in the presence of pyridine in methylene chloride. In a similar way, the isobutylate 1f, mp 65.5-66.5 °C (from hexane) (lit.,^{4a} mp 61-62 °C), and the 3,3-dimethylacrylate 1g, mp 79-82 °C (from hexane) (lit.,^{4a} mp 71-72 °C), were prepared quantitatively by treatment of 1d with isobutyryl and 3,3-dimethylacryloyl chlorides, respectively. Although the melting points of the synthesized esters are higher than those of natural products,^{4a} spectroscopic data of these esters of the both origins are well consistent with each other.

The tiglate 1h, mp 72.5-73 °C (from hexane) (lit.,¹³ mp 61-62 °C), was obtained in 96% yield by condensation of 1d with tiglic acid using *N,N'*-dicyclohexylcarbodiimide (DCC) and 4-pyrrolidinopyridine¹⁴ in chloroform at room temperature. The reaction of 1d with angelic acid under the above conditions, however, afforded a mixture of angelate 1i and tiglate 1h in a ratio of about 9:1 in 71% yield because of the isomerization of angelic acid or the ester 1i during the reaction. Pure ester 1i, mp 82.5-83 °C (lit.,^{4a} mp 83-84 °C), was easily obtained by purification with column chromatography followed by recrystallization from hexane.

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8. When the pyrolysis was carried out in a small scale (~10 mmol) and in a more dilute solution, a better yield of 1a is obtained; the maximum yield of a mixture of 1a and 1a' is up to 85%. 1a and 1a' (mp 64-65 °C) are separable by column chromatography on alumina.
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11. This compound could not be isolated in a pure form from *Eclipta erecta*.^{4a}
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13. The tiglate 1h could not be isolated in a pure form from *Eclipta erecta*,^{4a} and thus the reported melting point is that of the impure ester. However, the ¹HNMR spectra of the both esters coincided each other.
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