

2,5-DI(2'-THIENYL)FURAN AND AN IMPROVED SYNTHESIS OF  
ALPHA-TERTHIENYL

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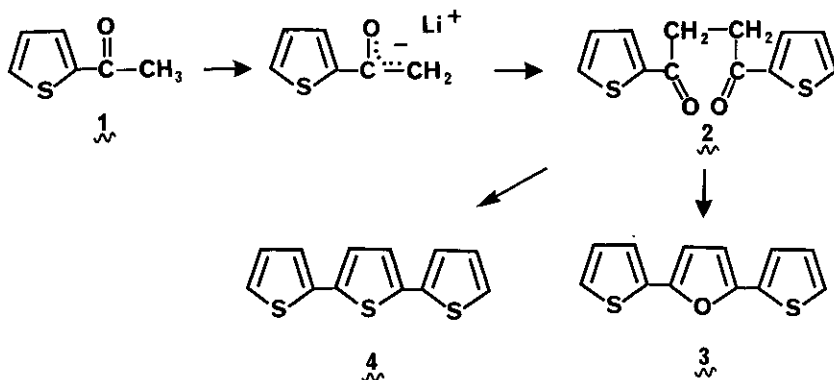
Abstract

The first synthesis of 2,5-di(2'-thienyl)furan was performed by oxidizing the lithium enolate of 2-acetylthiophene with cupric chloride, to 1,4-di(2'-thienyl)1,4-butanedione. This product was dehydrated with acetic anhydride in the presence of hydrogen chloride, to give the title compound in 74% overall yield. The same route provided a most convenient synthesis for alpha-terthienyl, which was obtained in 73% yield from 2-acetylthiophene.

Alpha-terthienyl (4) is a powerful photosensitizing agent.<sup>1</sup> The desire to study a structure-activity relationship created a need for the closely related molecule (3) in which the central thiophene ring was replaced by a furan ring. This molecule and its derivatives were unknown, and we describe an efficient synthesis for the parent compound, which should be applicable to the synthesis of many of its derivatives.

The acid-catalyzed dehydration of 1,4-diketones is a classical method for the synthesis of furans, which has also been applied recently to the preparation of alpha-terfuran.<sup>2</sup> Among the many syntheses of 1,4-diketones available, a particularly attractive one involves the oxidation of the lithium enolate of a methyl ketone, which has been applied to a related acetylfuran.<sup>3</sup>

The conversion of 2-acetylthiophene (1) to 1,4-di(2-thienyl)-1,4-butanedione (2) has been previously reported, utilizing the trimethylsilyl enol ether as an intermediate, and oxidizing it with silver oxide.<sup>4</sup> In our hands, the procedure described below, utilizing the oxidation of the enolate ion with  $\text{CuCl}_2$ , was found to be more convenient and to give a higher yield than that based on the  $\text{Ag}_2\text{O}$  oxidation of the trimethylsilyl enol ether.



n-Butyllithium (0.05 mol, 1.5 M in hexane) was added dropwise to a stirred solution of diisopropylamine (5.050 g, 0.05 mol) in dry THF (10 ml) at  $-78^\circ\text{C}$  under nitrogen. After 15 min, 2-acetylthiophene (5.670 g, 0.045 mol) was added dropwise at the same temperature. The mixture was stirred for 30 min, and anhydrous  $\text{CuCl}_2$  (6.720 g, 0.050 mol) in 15 ml of dry DMF was added in one portion. The dark green solution was stirred for an additional 40 min at  $-40^\circ\text{C}$ , and allowed to return to room temperature. It became homogeneous within 90 min. After addition of 50 ml of 3% hydrochloric acid, the mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (4 x 50 ml). The organic phase was washed with 3% HCl (3 x 10 ml), with water (3 x 10 ml), and was dried over  $\text{MgSO}_4$  and concentrated. The residue was flash chromatographed over silica gel, using ethyl acetate-hexane (1:4), to yield 4.76 g (85%) of 2, mp  $133-134^\circ\text{C}$  (lit mp  $130-131^\circ\text{C}^5$ ); IR ( $\text{CHCl}_3$ )  $1640\text{ cm}^{-1}$ ; nmr ( $\text{CDCl}_3$ ) 3.3 (s, 4 H), 7.0-7.8 ppm (m, 6 H); mass spec m/e 250 ( $\text{M}^+$ , 100%).

A stirred solution of 2 (100 mg) in acetic anhydride (5 ml) was treated with HCl gas at room temperature for 2 h, and was poured into ice water. After extraction with  $\text{CH}_2\text{Cl}_2$ , the organic phase was washed with water (4 x 10 ml), dried over  $\text{MgSO}_4$ , and concentrated. The residue was flash chromatographed over silica gel using hexane, and yielded 80 mg (87% yield) of 3, mp  $81-82^\circ\text{C}$ , nmr ( $\text{CDCl}_3$ ) 6.43 (s, 2 H) and 6.90-7.36 ppm (m, 6 H); mass spectrum: m/e 232 ( $\text{M}^+$ , 100%). Analysis. Calculated for

$C_{12}H_8OS_2$ : C, 62.04; H, 3.47; S, 27.60. Found: C, 61.78; H, 3.46; S, 27.42.

We also treated the diketone 2 with hydrogen sulfide and hydrogen chloride to complete a synthesis of alpha-terthienyl (4), which was obtained in 73.1% yield from 1, comparing favorably with the reported yields of 48%<sup>4</sup> and 23.9%<sup>5</sup> for the same conversion by other routes. We found this synthesis to be the most expeditious for preparing alpha-terthienyl from a readily available starting material.

ACKNOWLEDGMENTS We are grateful to the National Institutes of Health (GM 24144) for financial support.

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Received, 21st June, 1983