Pergamon

Tetrahedron Letters 41 (2000) 8461–8465

TETRAHEDRON LETTERS

Preparation of 3,4-di-*t*-butylthiophene 1-imide and its *N*-substituted derivatives

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Received 3 August 2000; revised 25 August 2000; accepted 1 September 2000

Abstract

Treatment of 3,4-di-*t*-butylthiophene 1-oxide with $(CF_3CO)_2O$ or $(CF_3SO_2)_2O$, followed by reaction with RSO_2NH_2, $ROC(=O)NH_2$, or $RCONH_2$ furnished a series of 1-imino derivatives of 3,4-di-*t*-butylthiophene, which carry an electron-withdrawing substituent on the imino nitrogen atom. Treatment of an imino derivative (substituent on the nitrogen atom = $CO_2{}^t$Bu) with CF_3CO_2H gave the corresponding aminosulfonium salt, whose deprotonation led to the *N*-unsubstituted parent 1-imide derivative.

Keywords: thiophenes; sulfimides/sulfilimines; sulfonium salts.

The chemistry of sulfilimines has been investigated from a variety of standpoints such as development of new syntheses, structures, reactivities, and applications to organic synthesis.[1] As for sulfilimine derivatives of monocyclic thiophenes, only a few derivatives have been synthesized to date.[2–4] The sulfilimines of this class would be of much importance as cyclic dienes. Their chemistry is also of interest in comparison with that of thiophene 1-oxides, which have attracted much attention recently.[5] We have previously shown that treatment of 3,4-di-*t*-butylthiophene (**1**) with TsN=IPh in the presence of a Cu(I) catalyst furnishes the 1-imino derivative (**2a**), 1,1-diimino derivative (**3**), and some other compounds.[3] However, we were frustrated at the following three drawbacks of the method: (1) the isolation procedure of **2a** is laborious because of the formation of many products; (2) the reaction required the use of twenty molar amounts of **1** to obtain **2a** in 61% yield, and (3) by conventional detosylation methods, **2a** was not converted to the *N*-unsubstitued parent compound (**6**), which is isolectronic with the corresponding thiophene 1-oxide and whose reactivities are expected to largely differ from those of the *N*-substituted compounds. These prompted us to develop an alternative synthesis of **2a** and related compounds by using 3,4-di-*t*-butylthiophene 1-oxide (**4**) as the starting material, which was easily prepared in good yield by oxidation of the thiophene **1** with *m*-chloroperbenzoic acid in the presence of $BF_3{\cdot}Et_2O$ and is kinetically stabilized by steric protection.[6,7]

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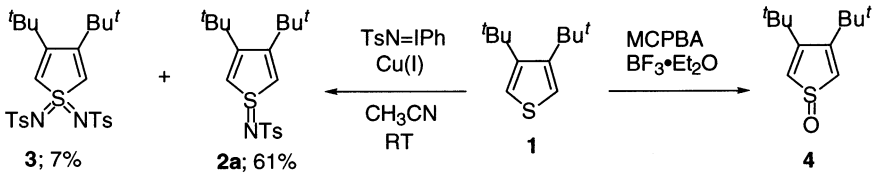
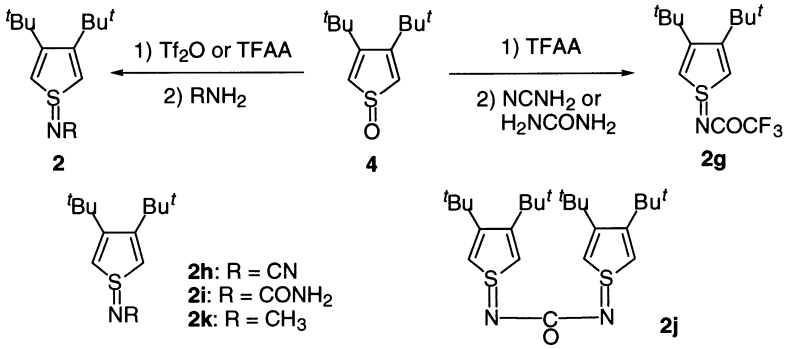
0040-4039/00/$ - see front matter
PII: S0040-4039(00)01481-7



The 1-oxide **4** (1 mmol) was treated with two molar amounts of $(CF_3CO)_2O$ (TFAA) at −78°C. *p*-Toluenesulfonamide (2 mmol) was added to this mixture at the same temperature. The resulting mixture was warmed slowly to room temperature, and the reaction was quenched by addition of aqueous Na_2CO_3. The mixture was worked up in the usual manner and purified by silica-gel column chromatography to give **2a** in 86% yield (Table 1, run 1).[8] The reaction, in which $(CF_3SO_2)_2O$ (Tf_2O) was used instead of TFAA under similar conditions, also afforded **2a** in 79% yield (run 2). Under these conditions, a series of derivatives **2a**–**f** were synthesized in satisfactory yields, as shown in Table 1.[8]

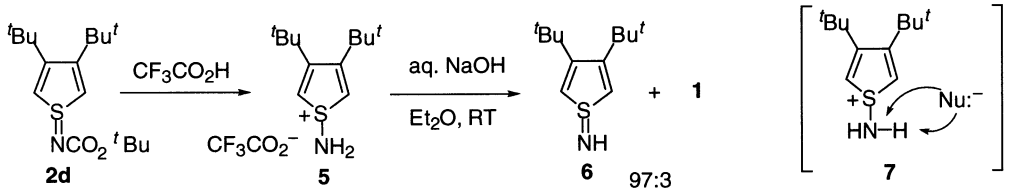
Table 1
Preparation of *N*-substituted 1-imino derivatives **2** of 3,4-*t*-butylthiophene



Run	1-Imino derivative	R	Acid anhydride	Yield (%)
1	**2a**	$SO_2C_6H_4CH_3(p)$	TFAA	86
2	**2a**	$SO_2C_6H_4CH_3(p)$	Tf_2O	79
3	**2b**	$SO_2C_6H_5$	Tf_2O	74
4	**2c**	CO_2Et	TFAA	90
5	**2d**	$CO_2{}^tBu$	TFAA	82
6	**2e**	$COCH_3$	TFAA	53
7	**2f**	$COC_6H_4CH_3$	TFAA	74

Although the above synthesis was quite satisfactory in many cases, unsatisfactory but interesting exceptions were found. Treatment of **4** with TFAA and then with H_2NCN yielded the trifluoroacetyl derivative (**2g**) in 85% yield, but not the expected cyano derivative (**2h**).[8] Similarly, treatment of **4** with TFAA and then with H_2NCONH_2 also gave **2g** in 83% yield. Neither of the expected **2i** or **2j** was formed. An analogy of the present reaction is found in the reaction of DMSO with TFAA and then with H_2NCONH_2 in CH_2Cl_2, which gave $Me_2S{=}NCOCF_3$ in 80% yield.[9] The reaction of **4** with $MeNH_2$, after treatment with TFAA, also failed to give the expected derivative (**2k**) with quantitative recovery of **4**.

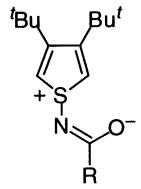
In order to obtain the *N*-unsubstituted parent compound (**6**), **2d** was treated with CF_3CO_2H.[10] The reaction satisfactorily yielded the aminosulfonium salt (**5**) quantitatively, which is the first aminosulfonium salt of thiophenes.[11] Treatment of a suspension of **5** in ether with aqueous NaOH gave the expected 1-imide **6** and the thiophene **1** in the ratio 97:3 quantitatively, whereas treatment of **5** with NaH in ether gave **6** and **1** in the ratio 58:42.[12] The formation of **1**, in addition to **6**, indicates that nucleophiles attack not only the amino hydrogen atom but also the amino nitrogen atom (**7**); in other words, **5** possesses potential to serve as an amination reagent. Compound **6** provides the first example of *N*-unsubstituted 1-imino derivatives of thiophenes. The 1-imide **6** is storable at below −20°C at least for one month without any appreciable decomposition, but it decomposed to thiophene **1** quantitatively through an unknown mechanism when its $CDCl_3$ solution was heated at 50°C for 6 h. It was converted into **2a** quantitatively by treatment with TsCl, thus suggesting that a variety of *N*-substituted compounds would be derived from **6**, if necessary.



The most characteristic features of the structure of **2** are found in their IR spectra.[13] The carbonyl stretching vibrations appear in abnormally low frequency ranges (Table 2). In particular, the carbonyl stretching vibration of **2f** appears at a frequency as low as 1541 cm^{-1}. This indicates that the 1,3-dipolar canonical structure **8** is the most suitable expression of the structure of these compounds.

Fig. 1 summarizes the chemical shift values (δ) in the ^1H and ^{13}C NMR spectra of **1** and its *S*-heteroatom-substituted derivatives **4**, **6**, **9**, and **10**.[14] The higher chemical shift value of the α-hydrogen atoms of **6** (δ 6.81), compared with that of **1** (δ 7.16), would be indicative of the loss of the aromaticity (ring current effect) of the thiophene ring of **6**, as was true of the 1-oxide **4**.[7] Interestingly, the α-hydrogen atoms of **4** and **6** resonate at lower fields than those of **9** and **10**, where two electronegative heteroatoms are bound to the sulfur atom. Finally, it would be worthy of mention that the α-carbon atom peaks of **4** and **6** appeared at lower fields than the corresponding peaks of **9** and **10** in the ^{13}C NMR spectra.

Table 2
Carbonyl stretching vibrations of **2c–g** in the IR spectra



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Compounds	**2c**	**2d**	**2e**	**2f**	**2g**
$\nu_{C=O}$ (cm^{-1})	1636	1639	1573	1541	1627

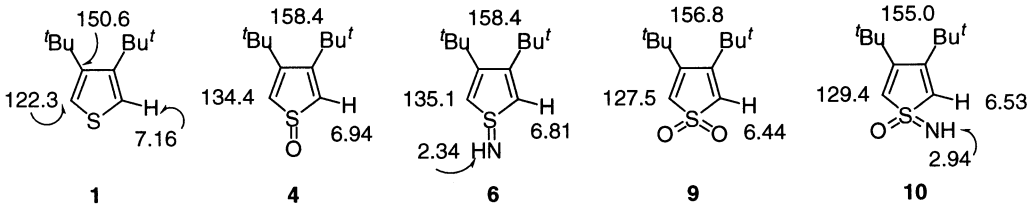

Figure 1. ^{1}H and ^{13}C NMR spectra of **1** and its 1-heteroatom-substituted derivatives (chemical shift was expressed in δ values)

Acknowledgements

T.O. thanks the Japanese Society for the Promotion of Science for Young Scientists for a Research Fellowship.

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8. Compound **2b**: mp 133–135°C; ^{1}H NMR (400 MHz, $CDCl_3$) $\delta=1.37$ (s, 18H), 6.70 (s, 2H), 7.43–7.53 (m, 3H), 7.88–7.90 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta=31.8$, 36.5, 126.9, 128.3, 128.6, 131.6, 143.2, 162.0. Compound **2c**: viscous oil; ^{1}H NMR (400 MHz, $CDCl_3$) $\delta=1.27$ (t, $J=7.1$ Hz, 3H), 1.42 (s, 18H), 4.13 (q, $J=7.1$ Hz, 2H), 6.92 (s, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta=14.7$, 32.0, 36.5, 62.1, 128.5, 162.4, 166.0. Compound **2d**: mp 129–131°C; ^{1}H NMR (400 MHz, $CDCl_3$) $\delta=1.42$ (s, 18H), 1.49 (s, 9H), 6.92 (s, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta=28.4$, 32.0, 36.4, 79.4, 128.8, 162.2, 165.6. Compound **2e**: mp 90–91°C; ^{1}H NMR (400 MHz, $CDCl_3$) $\delta=1.44$ (s, 18H), 2.14 (s, 3H), 7.10 (s, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta=23.4$, 31.9, 36.5, 126.9, 162.7, 182.1. Compound **2f**: mp 110–111°C; ^{1}H NMR (400 MHz, $CDCl_3$) $\delta=1.46$ (s, 18H), 2.37 (s, 3H), 7.16 (d, $J=8.0$ Hz, 2H), 7.22 (s, 2H), 7.97 (d, $J=8.0$ Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta=21.5$, 32.1, 36.6, 127.4, 128.6, 128.8, 132.8, 141.0, 162.4, 177.4. Compound **2g**: mp 158–160°C; ^{1}H NMR (400 MHz, $CDCl_3$) $\delta=1.46$ (s, 18H), 7.15 (s, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta=31.8$, 36.9, 117.0 (q, $^{1}J(C,F)=286$ Hz), 125.2 (dt, $^{5}J(C,F)=19$, 86 Hz), 164.7, 167.3 (q, $^{2}J(C,F)=35$ Hz).
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11. Compound **5**: mp 89–94°C (decomp.); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta=1.44$ (s, 18H), 6.97 (s, 2H), 7.16 (broad s, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta=31.7$, 37.0, 116.7 (q, $^{1}J(C,F)=294$ Hz), 126.5, 161.8 (q, $^{2}J(C,F)=34$ Hz), 165.7.

12. Compound **6**: viscous oil (solidifies in a refrigerator); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 1.44$ (s, 18H), 2.34 (broad s, 1H), 6.81 (s, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) $\delta = 32.1$, 35.9, 135.1, 158.4.
13. The S=N stretching vibrations of **2c**–**g** were not assigned in an unambiguous manner. Ab initio MO calculations of the 1-acetylimino derivative of the parent thiophene (C_4H_4S=NCOMe) at the B3LYP/6-31G* level predicted that the C=O stretching vibration appears at 1592 cm^{-1} as an intense band, while the S=N stretching vibration at 586 cm^{-1} appears as a weak band (scaling factor, 0.96). We thank Dr. A. Sakamoto of our department for the calculations.
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