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4,5- AND 3,5-BIS(ETHOXYCARBONYL)-2,7-DI-t-BUTYLTHIEPINES. SYNTHESIS AND THERMAL STABILITIES

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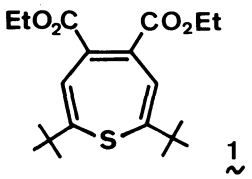
4,5-Bis(ethoxycarbonyl)-2,7-di-t-butylthiepine and 3,5-bis-(ethoxycarbonyl)-2,7-di-t-butylthiepine have been synthesized. Thermal stabilities of these thiepines have been examined and discussed in connection with those of the monocyclic thiepines reported so far.

Our continuous studies[1-4] on the monocyclic thiepines stabilized by two bulky t-butyl groups at C_2 and C_7 positions have revealed that the sulfur extrusion reaction of the thiepines proceeded with great facility when two additional substituents, either electron donating or electron withdrawing, were present at both C_4 and C_5 positions. Namely, 4-ethoxycarbonyl-5-methyl- and 4,5-dimethyl-2,7-di-t-butylthiepines have been shown to be less stable than the corresponding mono substituted 2,7-di-t-butylthiepines such as 4-ethoxycarbonyl and 4-methyl derivatives (see Table 1). Thus, the thiepines possessing these 4,5-substituents were prone to prefer thianorcaradiene proposed for an intermediate of the sulfur extrusion reaction.[5] We assumed that this acceleration can be explained in terms of their steric effect. For confirmation of this simple assumption and understanding of the thermal stability of the monocyclic thiepines, it is of interest to probe whether two electron withdrawing groups at C_4 and C_5 positions would facilitate or retard the sulfur extrusion reaction. We now wish to report the synthesis and properties of 4,5-bis(ethoxycarbonyl)-2,7-di-t-butylthiepine (**1**) together with those of 3,5-bis(ethoxycarbonyl)-2,7-di-t-butylthiepine (**2**).



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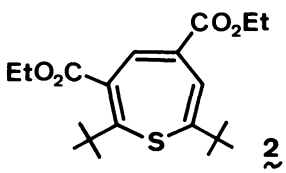
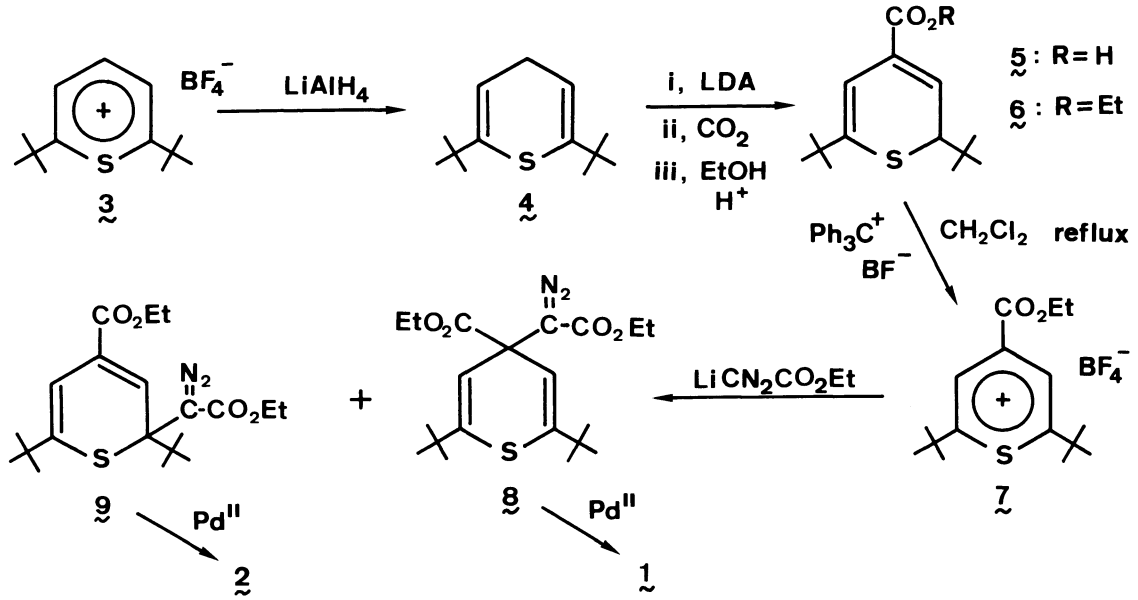


2

Although conversion of 4-ethoxycarbonyl-2,7-di-t-butyl-5-methylthiepine into **1** by transformation of the methyl group has not met with success, **1** could be prepared keeping our previous synthetic strategy in mind. 2,6-Di-t-butylthiopyrylium tetrafluoroborate (**3**)[3] was reduced ($LiAlH_4$, ether, 25 °C, overnight) quantitatively to a mixture of 2,6-di-t-butyl-4H-thiopyran (**4**)[3] and its 2H-isomer[3] as a colorless oil which can be used in the next step without separation. Treatment of the mixture with lithium diisopropylamide in tetrahydrofuran in the presence of HMPA at -60 °C under nitrogen followed by dry carbon dioxide gave the carboxylic acid **5**, which was converted into the ethyl ester **6** (C_2H_5OH/H_2SO_4). The compound **6**, a pale yellow oil, was fully characterized by the elemental analysis and the spectroscopic data: ^{1}H-NMR (100 MHz, $CDCl_3$) δ 6.55 (d, J = 6.5 Hz, 1H), 6.47 (s, 1H), 4.24 (q, J = 7.1 Hz, 2H), 3.36 (d, J = 6.5 Hz, 1H), 1.32 (t, J = 7.1 Hz, 3H), 1.24 (s, 9H), 0.98 (s, 9H); IR (neat) 1720 cm^{-1} (C=O). Since the thiopyran **6** has an electron withdrawing ethoxycarbonyl group, it could not be converted into the thiopyrylium ion **7** under the usual conditions. The hydride abstraction of **6**, however, was performed under drastic conditions. Thus, on treatment with triphenylmethyl tetrafluoroborate in dichloromethane under reflux for 24 h, **6** was



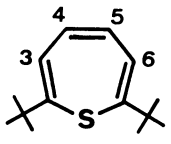
converted into **7** in 66% yield: colorless prisms, mp 197.5-200.5 °C (decomp), ^{1}H-NMR (100 MHz, $CDCl_3$) δ 8.92 (s, 2H), 4.57 (q, J = 7.1 Hz, 2H), 1.67 (s, 18H), 1.49 (t, J = 7.1 Hz, 3H); IR (KBr) 1720 cm^{-1} (C=O), 1000-1200 cm^{-1} (BF_4^-).

Reaction of **7** with ethyl lithiodiazoacetate generated in situ from ethyl diazoacetate in a mixture of ether and tetrahydrofuran (1:1) by treatment with lithium

diisopropylamide gave a mixture of **8** and **9** in 78% yield, the ratio of which depend on the reaction conditions. Finally, the mixture of **8** and **9** was allowed to react with a catalytic amount of di-μ-chloro(η^3-allyl)palladium in chloroform at room temperature giving rise to a mixture of the thiepines **1** (major) and **2** (minor) in 75% yield which could be separated easily by column chromatography on silica gel with hexane-ether (5:1). The structures of **1** and **2** were confirmed through their elemental analyses and the spectral characteristics as follows: **1**, a pale yellow oil, ^{1}H-NMR (100 MHz, $CDCl_3$) δ 6.46 (s, 2H), 4.24 (q, J = 7.0 Hz, 4H), 1.30 (t, J = 7.0 Hz, 6H), 1.24 (s, 18H); ^{13}C-NMR (22.49 MHz, $CDCl_3$) δ 167.5, 157.5, 138.6, 125.8, 61.5, 40.4, 30.4, 14.0, UV (cyclohexane) λ_{max} nm (log ε), 238 (4.11), 380 (2.75); IR (neat) 1720 cm^{-1} (C=O); **2**, a pale yellow oil, ^{1}H-NMR (100 MHz, $CDCl_3$) δ 7.55 (s, 1H), 6.75 (s, 1H), 4.24 (q, J = 7.1 Hz, 2H), 4.23 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H), 1.32 (s, 9H), 1.31 (t, J = 7.1 Hz, 3H), 1.27 (s, 9H); ^{13}C-NMR (22.49 MHz, $CDCl_3$) δ 168.7, 166.1, 160.4, 153.2, 141.4, 136.0, 133.9, 126.8, 61.5, 61.1, 41.2, 40.2, 30.3, 14.2, 13.9; UV (cyclohexane) λ_{max} nm (log ε), 208 (4.27), 238 (4.00), 376 (2.79); IR (neat) 1720 cm^{-1} (C=O).

Thermolyses of **1** and **2** were carried out in a degassed toluene-d_8 and the reactions were monitored by ^{1}H-NMR spectroscopy. The thiepine **1** was converted to diethyl 4,5-di-t-butylphthalate[6] with half-life of 254 h at 130 °C, however, the isomeric thiepine **2** remained intact even for 1000 h at the same conditions. These results are summarized in Table 1 together with the previously reported data for the other monocyclic thiepines. Inspection of the data on half-lives of available monocyclic thiepines depicted in Table 1 it is apparent that the effect of substituents such as electron withdrawing ethoxycarbonyl group and electron donating methyl group on the thermal stability of monocyclic thiepine is more com-

Table 1. Half-lives (h) of substituted 2,7-di-t-butylthiepines at 130 °C in toluene-d_8



3,5-$(CO_2Et)_2$	parent	4,5-$(CO_2Et)_2$	4-CO_2Et	4-CH_3	4,5-$(CH)_3$	4-CO_2Et-5-CH_3
>1000[a]	365[b]	254[a]	157[a]	105[a]	15[a]	7[c]

a) Present work. b) Ref. 3. c) Ref. 1.

plex than it seems at first glance.[7] The unexpected high stability of **2** can not be explained in terms of simple electronic and steric effects, however, the latter effect seems to be at least partly responsible for the thermal stability of the thiepine. For unified understanding of both the previous and the present findings, studies on the basis of sophisticated theoretical calculations have to be done in detail. These studies are now in progress and will be reported elsewhere.[8]

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6) Colorless plates, mp 64.0-65.5 °C, ^{1}H-NMR (100 MHz, $CDCl_3$) δ 7.93 (s, 2H), 4.34 (q, J = 7.2 Hz, 4H), 1.54 (s, 18H), 1.34 (t, J = 7.2 Hz, 6H); ^{13}C-NMR (22.49 MHz, $CDCl_3$) δ 167.8, 152.5, 130.4, 128.6, 61.2, 37.9, 34.3, 14.0; UV (cyclohexane) λ_{max} nm (log ε) 210 (4.59), 242 (4.03), 287 (3.26); IR (KBr) 1720 cm^{-1}.

7) Previously we have claimed that the 1-benzothiepine system is stabilized by electron donating methyl group whereas the reverse is true for π-accepting ethoxycarbonyl group except 2-substituted 1-benzothiepines. K. Nishino, K. Nakasuji, and I. Murata, Tetrahedron Lett., 1978, 3567.

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