Pergamon

Tetrahedron Letters, Vol. 38, No. 8, pp. 1431-1434, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00040-3

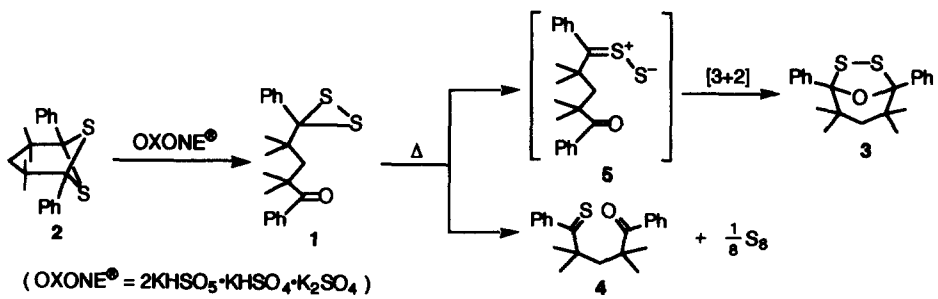
Preparation and Properties of a 3,3-Dialkyldithiirane

Akihiko Ishii, Kazuyo Umezawa, and Juzo Nakayama*

Department of Chemistry, Faculty of Science, Saitama University,
Urawa, Saitama 338, Japan

Abstract: Treatment of 1,5-di-*t*-butyl-2,2,4,4-tetramethyl-6,7-dithiabicyclo[3.1.1]heptane (**10**) with $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ in dichloromethane-water at room temperature gave the 3,3-dialkyldithiirane **6** as an orange oil. Oxidation of **6** gave a 1:1 mixture of the corresponding (1*RS*, 3*SR*)- (**13**) and (1*RS*, 3*RS*)- (**14**) dithiirane 1-oxides. Thermal reaction of the dithiirane **6** yielded the corresponding 8-oxa-6,7-dithiabicyclo[3.2.1]octane derivative **15** as the main product.

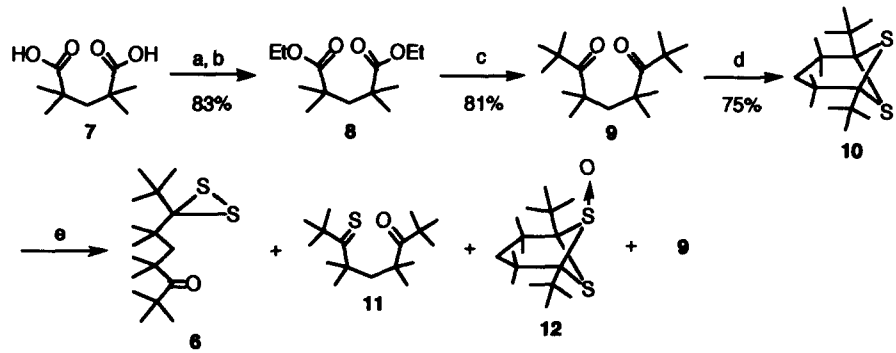
The chemistry of dithiiranes has drawn considerable attention because of their unique structure.[1,2] We have recently succeeded in the synthesis of the first isolable dithiirane, 3-phenyl-3-(1,1,3,3-tetramethyl-4-oxo-4-phenylbutyl)dithiirane (**1**), by the reaction of the 6,7-dithiabicyclo[3.1.1]heptane **2** with $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ (OXONE®).[3] When the dithiirane **1** was heated in solution, the 8-oxa-6,7-dithiabicyclo[3.2.1]octane **3** and the thioketone **4** were formed. We proposed that the compound **3** formed by an intramolecular [3+2] cycloaddition of the δ-thioxoketone *S*-sulfide **5**, while the thioketone **4** by a bimolecular process (Scheme 1).[3] The dithiirane **1** belongs to a class of 3-alkyl-3-aryldithiiranes, and it is therefore of great interest to investigate substituent effects on the stability of dithiirane rings in relation to the isomerization of dithiiranes to the corresponding thioketone *S*-sulfide (or the equilibrium between them).[1,4] We report here the preparation of the first 3,3-dialkyldithiirane derivative and its oxidation and thermal reactions.



Scheme 1

The dialkyldithiirane **6** was prepared as follows (Scheme 2). Thus, a solution of the dicarboxylic acid **7**[5] in DMSO was treated with aqueous NaOH and then with ethyl iodide[6] to give the diester **8**.[7] The diester **8** was

treated with *t*-BuLi in Et_2O at –50 °C to give the dicarbonyl compound **9** which was sulfurized with Lawesson's reagent[8] in refluxing toluene to yield the 6,7-dithiabicyclo[3.1.1]heptane **10**. A solution of the bicyclic compound **10** and $2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$ in CH_2Cl_2-H_2O was stirred vigorously at room temperature[9] to give a mixture of the desired dithiirane **6**, the thioketone **11**, the sulfoxide **12**, and **9**. The mixture was subjected to HPLC (SiO_2) to give the dithiirane **6** as an orange oil in 16% isolated yield.[10] In the ^{13}C NMR, the dithiirane ring carbon of **6** appeared at a lower field of δ 85.8 than that of the alkylaryldithiirane **1** (δ 80.6). The UV-Vis spectrum of the dithiirane **6** showed the absorption maximum at 453 nm which is very close to that of **1** (λ_{max} 452 nm).

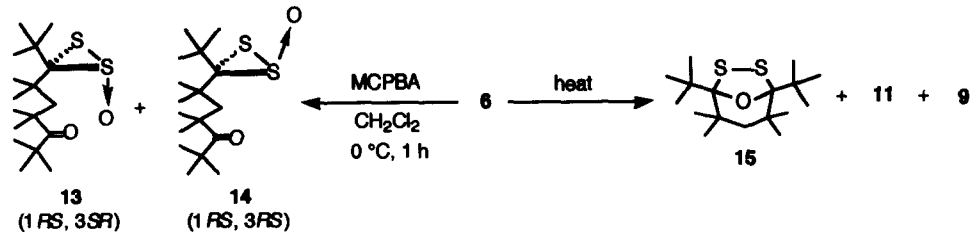


Reagents and Conditions: a, aqueous NaOH, DMSO, room temp.; b, EtI (8 molar amounts), room temp., 22 h; c, *t*-BuLi (2 molar amounts), Et_2O, –50 °C, 1 h; d, Lawesson's reagent (3.6 molar amounts), $PhCH_3$, reflux, 39 h; e, aqueous $2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$ (12.5 equiv), CH_2Cl_2, room temp., 10 h.

Scheme 2

Oxidation and thermal reactions of the dithiirane **6** were examined (Scheme 3). The oxidation of the dithiirane **6** with MCPBA was carried out in CH_2Cl_2 at 0 °C for 1 h. The ^1H-NMR spectrum of the reaction mixture showed the formation of the corresponding (1*RS*, 3*SR*)- (**13**) and (1*RS*, 3*RS*)- (**14**) dithiirane 1-oxides in the molar ratio of 1:1. Purification of the mixture by column chromatography (SiO_2) gave a 1:1 mixture of **13** and **14** in 87% combined yield. The 1:1 mixture was subjected to HPLC (SiO_2) to give pure **13** and **14** in 17 and 19% yields, respectively, where about a half amount of **13** and **14** decomposed in the HPLC column used. The stereochemistry of the two isomeric dithiirane 1-oxides were elucidated on the basis of ^1H-NMR analysis[10] in analogy with two isomeric dithiirane 1-oxides (**16** and **17**) of the dithiirane **1**;[3b,e] the criterion is that one of the two α-methyls, trans to the sulfoxide oxygen atom, resonates at a higher field characteristically owing to the anisotropic effect of the S=O group. The dithiirane 1-oxides **13** and **14** were oily materials and stable in a dilute solution but some isomerization and decomposition to the corresponding thioketone *S*-oxide **18**[11] and **9** were observed on standing the neat oils in a refrigerator for 3 days; pure **13** and **14** became mixtures of **13**, **14**, **18**, and **9** in the molar ratios of 65:23:10:2 and 16:66:17:1, respectively.

Heating the dithiirane **6** in refluxing 1,2-dichloroethane for 48 h gave a mixture of the corresponding 8-oxa-6,7-dithiabicyclo[3.2.1]octane **15**, **11**, **9** and **6** in the molar ratio of 83:13:2:2 (Table 1, Run 1). Change of the solvent from 1,2-dichloroethane to benzene decreased the yield of **15** (**15**:**11** 57:43, Run 2), which is a tendency similar to the case of the dithiirane **1**. Thus, for δ-oxodithiiranes such as **6** and **1**, thermal



Scheme 3

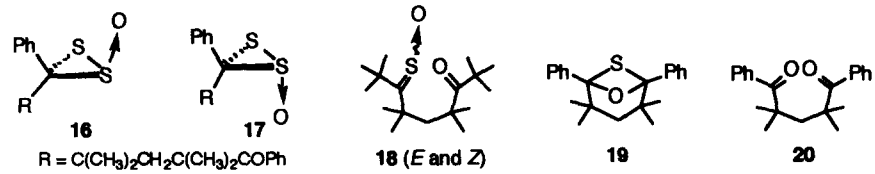


Table 1. Thermal Reaction of Dithiiranes **6** and **1**.[a]

Run	Dithiirane	Solvent	c / mol dm^{-3}	Temp.	Time / h	Products (molar ratio)[b]			
						15 or **3**	**11** or **4**	Others	Recovery
1	*t*-Bu (**6**)	$(ClCH_2)_2$	3.2×10^{-4}	refl.	48	83 (**15**)	13 (**11**)	2 (**9**)	2 (**6**)
2	*t*-Bu (**6**)	C_6H_6	3.2×10^{-4}	refl.	48	57 (**15**)	43 (**11**)	–	–
3	*t*-Bu (**6**)	$CDCl_3$	1.2×10^{-2}	60 °C	67	83 (**15**)	5 (**11**)	2 (**9**)	10 (**6**)
4	Ph (**1**)	$CDCl_3$	1.2×10^{-2}	60 °C	67	26 (**3**)	15 (**4**)	2 (**19**)	57 (**1**)

a: All runs were carried out under an argon atmosphere. b: Determined by ^{1}H NMR.

isomerization to the corresponding 8-oxa-6,7-dithiabicyclo[3.2.1]octanes is a common reactivity and is in competition with desulfurization giving thioketones.

In the thermal isomerization, the ring opening of δ-oxodithiiranes to δ-thioxoketone *S*-sulfides is the rate-controlling step because the δ-thioxoketone *S*-sulfides would instantly cyclize to the corresponding 8-oxa-6,7-dithiabicyclo[3.2.1]octanes, and therefore the relative rate of the isomerization is a good measure for the stability of dithiirane rings. On the other hand, the low efficiency of desulfurization of dithiiranes yielding thioketones indicates the effective steric protection by the substituents because the thioketones are considered to be formed by a bimolecular process.[12] When a $CDCl_3$ solution of the dialkyldithiirane **6** was heated at 60 °C in an NMR tube, 90% of **6** was consumed after 67 h and the molar ratio of **15**:**11**:**9**:**6** was 83:5:2:10 (Run 3). Under similar conditions, only 43% of alkylaryldithiirane **1** was consumed and the molar ratio of **3**:**4**:**19**:**20**:**1** was 26:15:2:trace:57 (Run 4), indicating that decomposition of the dithiirane **6** is much faster than that of **1**. These substituent effects can be explained in terms of the inductive effect of the substituents: the electron-releasing *t*-butyl group destabilizes the HOMO level of the dithiirane ring,[2a] while the electron-withdrawing phenyl group provides the opposite effect. On the other hand, the *t*-butyl group in **6** exerts as a better steric protecting group than the phenyl group in **1** since the ratio of the formation of 8-oxa-6,7-dithiabicyclo[3.2.1]octane to that of thioketone is much higher for **6** than that for **1**.

REFERENCES AND NOTES

1. For reviews, see: Senning, A.; Hansen, H. C.; Abdel-Megeed, M. F.; Mazurkiewicz, W.; Jensen, B. *Tetrahedron* **1986**, 42, 739-746; Senning, A. *Sulfur Lett.* **1986**, 4, 213-216; Senning, A. *Sulfur Lett.* **1990**, 11, 83-86.
2. a) Snyder, J. P.; Carlsen, L. *J. Am. Chem. Soc.* **1977**, 99, 2931-2942. b) So, S. P. *J. Mol. Struct. (Theochem)*, **1986**, 148, 153-161.
3. a) Ishii, A.; Akazawa, T.; Maruta, T.; Nakayama, J.; Hoshino, M.; Shiro, M. *Angew. Chem. Int. Ed. Engl.* **1994**, 33, 777-779. b) Ishii, A.; Akazawa, T.; Ding, M.-X.; Honjo, T.; Nakayama, J.; Hoshino, M.; Shiro, M. *J. Am. Chem. Soc.* **1993**, 115, 4914-4915. c) Ishii, A.; Jin, Y.-N.; Nagaya, H.; Hoshino, M.; Nakayama, J. *Tetrahedron Lett.* **1995**, 36, 1867-1870. d) Ishii, A.; Maruta, T.; Teramoto, K.; Nakayama, J. *Sulfur Lett.* **1995**, 18, 237-242. e) Ishii, A.; Akazawa, T.; Ding, M.-X.; Honjo, T.; Maruta, T.; Nakamura, S.; Nagaya, H.; Ogura, M.; Teramoto, K.; Shiro, M.; Hoshino, M.; Nakayama, J. *Bull. Chem. Soc. Jpn.* in press.
4. Huisgen, R.; Rapp, J. *J. Am. Chem. Soc.* **1987**, 109, 902-903.
5. Maier, G.; Roth, C.; Schmitt, R. K. *Chem. Ber.* **1985**, 118, 704-721.
6. Pfeffer, P. E.; Foglia, T. A.; Barr, P. A.; Schmeltz, I.; Silbert, L. S. *Tetrahedron Lett.* **1972**, 4063-4066; Shaw, J. E.; Kunerth, D. C.; Sherry, J. J. *Tetrahedron Lett.* **1973**, 689-692. HMPA was employed as the solvent in the literatures.
7. Weagley, R. J.; Gibson, H. W. *Synthesis* **1986**, 552-554.
8. Pedersen, B. S.; Scheibye, S.; Nilsson, N. H.; Lawesson, S.-O. *Bull. Soc. Chim. Belg.* **1978**, 87, 223-228.
9. The pH of the aqueous layer was adjusted to 6 every 2 h by addition of 1M KOH.
10. All new compounds gave satisfactory analytical or HRMS data. Selected physical and spectral data: dithiirane **6**: orange oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.20 (s, 6H), 1.26 (s, 9H), 1.34 (s, 9H), 1.35 (s, 6H), and 2.29 (s, 2H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 29.1, 29.5, 29.6, 33.3, 42.5, 46.5, 46.8, 50.9, 53.8, 85.8 (S-*C*-S), and 218.5 (C=O); UV-Vis (CH_2Cl_2) λ_{max} 453 nm (ε 55); MS (70 eV) *m/z* 316 (M^+, 3), 284 (4), 252 (4), 27 (9), 199 (8), 183 (60), and 57 (100); thioketone **11**: purple oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.22 (s, 6H), 1.26 (s, 9H), 1.39 (s, 6H), 1.50 (s, 9H), and 2.54 (s, 2H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 29.0, 29.1, 32.6, 33.8, 46.4, 50.1, 53.4, 54.3, 57.7, 218.7 (C=O), and 279.0 (C=S); MS (70 eV) *m/z* 284 (M^+, 5), 227 (6), 199 (7), 183 (48), and 57 (100); (1*RS*, 3*SR*)-dithiirane 1-oxide **13**: colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.13 (s, 9H), 1.28 (s, 9H), 1.30 (s, 3H), 1.31 (s, 6H), 1.47 (s, 3H), 2.26 (d, J = 14 Hz, 1H), and 2.84 (d, J = 14 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 28.1 (Me), 28.9 (*t*-Bu), 29.9 (*t*-Bu), 30.8 (Me), 30.9 (Me), 31.4 (Me), 41.9 (C), 46.52 (C), 46.54 (C), 49.2 (CH_2), 50.6 (C), 88.7 (S-*C*-S), and 218.9 (*C*=O); MS (30 eV) *m/z* 333 (M^++1, 1.1), 332 (M^+, 0.7), 316 (3), 300 (23), 211 (58), 183 (75), and 57 (100); (1*RS*, 3*RS*)-dithiirane 1-oxide **14**: colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.76 (s, 3H), 1.17 (s, 3H), 1.24 (s, 9H), 1.31 (s, 3H), 1.35 (s, 3H), 1.45 (s, 9H), 1.96 (d, J = 14 Hz, 1H), and 2.34 (d, J = 14 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 26.5 (Me), 28.2 (Me), 28.9 (*t*-Bu), 29.6 (Me), 29.8 (Me), 32.8 (*t*-Bu), 41.7 (C), 46.3 (C), 46.5 (C), 50.1 (C), 51.2 (CH_2), 88.7 (S-*C*-S), and 218.0 (*C*=O); MS (30 eV) *m/z* 333 (M^++1, 1.5), 332 (M^+, 0.8), 316 (2), 300 (23), 211 (79), 183 (98), and 57 (100); **15**: pale yellow needles, m.p. 114—115 °C (hexane). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.68 (d, J = 14 Hz, 1H), 1.28 (s, 6H), 1.32 (s, 18H), 1.41 (s, 6H), and 2.49 (d, J = 14 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 29.5, 31.0, 31.7, 43.7, 44.6, 59.0, and 122.7; MS (70 eV) *m/z* 316 (M^+, 41), 284 (2), 252 (42), 112 (100), and 57 (77).
11. Determination of the geometry of the *E*- and *Z*- thioketone *S*-oxide will be discussed elsewhere.
12. Chew, M.; Harpp, D. N. *Tetrahedron Lett.* **1992**, 33, 45-48.

(*Received in Japan* 28 *November* 1996; *revised* 26 *December* 1996; *accepted* 6 *January* 1997)