Chemistry of 1,3-Oxathianes. Reactivity of 2-Heterosubstituted 1,3-Oxathianes toward *sec*-Butyllithium and the Reaction of 2-(Trimethylsilyl)-1,3-oxathianyl Anion with Electrophiles[1,2]

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Received November 3, 1983

Investigation on the reaction of 2-heterosubstituted 1,3-oxathianes with *sec*-BuLi disclosed that all three possible reaction pathways, i, abstraction of the proton at C(2), ii, nucleophilic displacement at C(2), and iii, nucleophilic attack at the heteroatom, occurred depending on the heteroatom at C(2). With 2-(trimethylsilyl)-1,3-oxathiane (**1a**), *sec*-BuLi acts as a base to produce the corresponding anion **1b**, whose reaction with electrophiles affords a variety of 2,2-disubstituted products. The reaction of 2-(trimethylsilyl)-1,3-oxathianyl anion (**1b**) with benzonitrile followed by hydrolysis gave rise to 2-benzoyl-1,3-oxathiane (**17**) instead of the expected 2-benzoyl-2-(trimethylsilyl)-1,3-oxathiane (**16**). Consideration of the mechanism for the formation of **17** has resulted in the development of an equivalent of acyl dianion generated from 1 molar equiv of base.

Introduction

Although much knowledge of the chemistry of 2-heterosubstituted 1,3-dithianes has accumulated,[3] 2-heterosubstituted 1,3-oxathianes have not received attention from synthetic organic chemists. We prepared a variety of 2-heterosubstituted 1,3-oxathianes[1] to examine their chemical properties with the initial intention to develop masked acyl anions in higher oxidation states, to increase the kinetic acidity of H(2),[4,5] to increase the softness of the resulting anion, and to reveal the reactivity characteristic of heteroatoms introduced at C(2). The substituents on the heteroatom were in all cases methyl to avoid complications arising from differing steric bulk.

Results

(1) The Reaction of 2-Heterosubstituted 1,3-Oxathianes with *sec*-BuLi. To a stirred solution of a given 2-heterosubstituted 1,3-oxathiane in tetrahydrofuran (THF) was added a hexane solution of *sec*-BuLi under nitrogen at −78 °C until the solution was colored faint yellow. After being stirred for a few minutes, the reaction mixture was quenched with D_2O and the products were analyzed. *sec*-BuLi reacted as a base with 2-(trimethylsilyl)- and 2-(trimethylgermyl)-1,3-oxathianes (**1a** and **2a**) to afford the corresponding 2-deuterio derivatives **1c** and **2c** through anions **1b** and **2b**, respectively. High yield recovery of the substrate and nearly quantitative incorporation of the deuterium atom at C(2) indicated the complete transformation of **1a** and **2a** into **1b** and **2b**, respectively. In contrast, with 2-(trimethylstannyl)- and 2-(trimethylplumbyl)-1,3-oxathianes (**3** and **4**) nucleophilic attack of *sec*-BuLi at the heteroatom took place to produce 1,3-oxathianyl anion **5a**. This was followed by deuteration to give 2-deuterio-1,3-oxathiane (**5b**) in high yield with quantitative incorporation of deuterium. None of 2-(group 16)-substituted[20] 1,3-oxathianes **6a**, **7a**, and **8a** afforded the corresponding anions **6b**, **7b**, and **8b** with *sec*-BuLi. 2-Methoxy- and 2-(methylthio)-1,3-oxathianes gave rise to 2-*sec*-butyl-1,3-oxathiane (**5c**)[6] in 57% and 14% yield, respectively. A 54% yield of 2-deuterio-1,3-oxathiane (**5b**) as well as **5c** (26%) was obtained from 2-(methylseleno)-1,3-oxathiane (**8a**). Attempted reaction of 2-(dimethylamino)-1,3-oxathiane (**9**) with *sec*-BuLi produced a complex mixture including starting material. 2-(Dimethylthiophosphinoyl)-1,3-oxathiane (**10a**)[7] was converted quantitatively to the corresponding anion **10b**, which was quenched with D_2O to afford the 2-deuterio dcerivative **10c**.

Table I. Reaction of 2-(Trimethylsilyl)-1,3-oxathianyl Anion (1b) with Various Electrophiles

electrophile	product	R	yield, %
MeI	**1d**	Me	86[a]
EtI	**1e**	Et	38[a]
i-PrI	**1f**	*i*-Pr	52[a]
i-BuI	**1g**	*i*-Bu	41[b]
$(MeS)_2$	**1h**	SMe	65[a]
PhCHO	**1i**	CH(OH)Ph	75[b,c]
PhCH=CHCHO	**1j**	CH(OH)CH=CHPh	76[b,c]
PhCOPh	**1k**	$C(OH)Ph_2$	46[b]

[a] Determined by GLC. [b] Isolated yield. [c] A mixture of two diastereoisomers.

(1) Chemistry of carbanions stabilized by sulfur 2. For the previous paper in this series, see: Fuji, K.; Ueda, M.; Sumi, K.; Kajiwara K.; Fujita, E.; Iwashita, T.; Miura, I. *J. Org. Chem.*, the preceding paper in this issue.

(2) A part of this work has been published in a preliminary form: Fuji, K.; Sumi, K.; Fujita, E. *Tetrahedron Lett.* **1981**, *22*, 2005. Fuji, K.; Ueda, M.; Fujita, E. *J. Chem. Soc., Chem. Commun.* **1983**, 49.

(3) For oxy derivatives: (a) Stutz, P.; Stadler, P. A. *Helv. Chim. Acta* **1972**, *55*, 75. (b) Yoshida, H.; Yoshikane, M.; Ogata, T.; Inokawa, S. *Synthesis* **1976**, 551. For thio derivatives: (c) Ellison, R. A.; Woessner, W. D., Williams, C. C. *J. Org. Chem.* **1972**, *37*, 2757. (d) Seebach, D.; Geiss, K. H.; Beck, A. K.; Graf, B.; Daum, H. *Chem. Ber.* **1972**, *105*, 3280. (e) Arai, K.; Oki, M. *Tetrahedron Lett.* **1975**, 2183. (f) Arai, K.; Oki, M. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 553. (g) Woessner, W. D. *Chem. Lett.* **1976**, 43 and ref 3b. For amino derivatives: (h) Hassner, A.; Munger, P.; Bellinka, Jr. B. A. *Tetrahedron Lett.* **1982**, *23*, 699 and ref 3e. For phosphonio derivatives: (i) Kruse, C. G.; Broekhof, N. L. J. M.; Wijsman, A.; van der Gen, A. *Tetrahedron Lett.* **1977**, 885. For silyl derivatives: (j) Brook, A. G.; Duff, J. M.; Jones, P. F.; Davis, N. R. *J. Am. Chem. Soc.* **1967**, *89*, 431. (k) Corey, E. J.; Seebach, D.; Freedman, R. *J. Am. Chem. Soc.* **1967**, *89*, 434. (l) Corey, F. A.; Court, A. S. *J. Org. Chem.* **1972**, *37*, 1926. (m) Jones, P. F.; Lappert, M. F. *J. Chem. Soc., Chem. Commun.* **1972**, 526. (n) Jones, P. F.; Lappert, M. F.; Szary, A. C. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2272. (o) Seebach, D.; Gröbel, B.-T.; Beck, A. K.; Braun, M.; Geiss, K. H. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 443. (p) Seebach, D.; Molb, M.; Gröbel, B.-T. *Chem. Ber.* **1973**, *106*, 2277. (q) Gröbel, B.-T.; Burstinghaus, R.; Seebach, D. *Synthesis* **1976**, 121. (r) Anderson, N. H.; McCrae, D. A.; Grotjahan, D. B.; Gabbe, S. Y.; Theodore, L. J.; Ippolito, R. M.; Sarkar, T. K. *Tetrahedron* **1981**, *37*, 4069. (s) Grotjahn, D. B.; Anderson, N. H. *J. Chem. Soc., Chem. Commun.* **1981**, 306. For germyl derivatives: ref 3j. For stannyl derivatives: (t) Seebach, D.; Willert, I.; Beck, A. K.; Gröbel, B.-T. *Helv. Chim. Acta* **1978**, *61*, 2510 and ref 3j and 3r. For borato derivatives: (u) Hughes, R. J.; Ncube, S.; Pelter, A.; Smith, K.; Negishi, E.; Yoshida, T. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1172. For chloro derivatives: (v) Kruse, C. G.; Wijsman, A.; van der Gen, A. *J. Org. Chem.* **1979**, *44*, 1847 and ref 12e, 12f, and 12i.

(4) Bordwell, F. G.; Puy, M. V. D.; Vanier, N. R. *J. Org. Chem.* **1976**, *41*, 1885.

(5) Kauffmann, T.; Altepeter, B.; Echsler, K. J.; Ennew, J.; Hamsen, A.; Joussen, R. *Tetrahedron Lett.* **1979**, 501.

(6) Ca. a 1:1 mixture of erythro and threo isomers determined by ^{13}C NMR.

(7) The corresponding tervalent phosphorus compound, (dimethylphosphino)-1,3-oxathiane, proved to be extremely unstable. It is oxidized rapidly on exposure to air.

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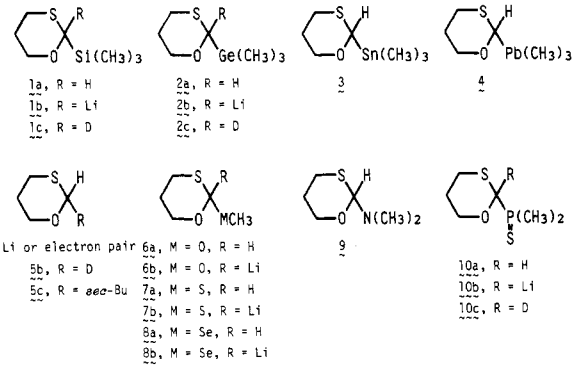
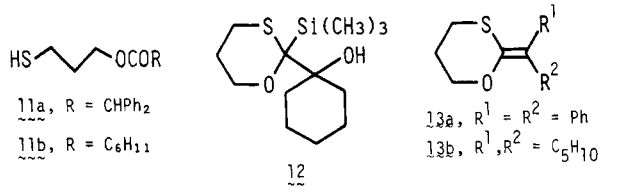
Except in the case of **10a**,[8] the starting 2-heterosubstituted 1,3-oxathianes were recovered unchanged in every case when lithium dicyclohexylamide was used instead of *sec*-BuLi.



(2) The Reaction of 2-Trimethylsilyl Anion 1b with Electrophiles. Products and yields of the reactions of **1b** with various electrophiles are listed in Table I. Exclusive 1,2-addition of **1b** to cinnamaldehyde was observed. In the reaction of benzophenone, ester **11a** was generated in 37% yield together with the expected product **1k**. Cyclohexanone afforded a simple adduct **12** at −78 °C. Warming up the reaction mixture to 20 °C yielded **11b** in 66% yield. Esters **11a** and **11b** were presumably formed through ketene *S,O*-acetals **13a** and **13b**, respectively.

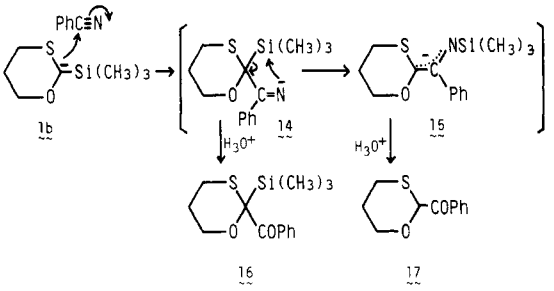


Unexpectedly, the reaction of benzonitrile with **1b** followed by acid hydrolysis gave rise to 2-benzoyl-1,3-oxathiane (**17**) in 73% yield instead of the expected product **16**. A plausible mechanism for the formation of **17** is shown in Scheme I. Electrophilic attack of benzonitrile on the anion **1b** produces an adduct **14**. This is followed by a C → N shift of the trimethylsilyl group[9] to give another anion **15**, which is quenched and hydrolyzed with acid to generate **17**. If this is the case, the anion **15** can be trapped by other electrophiles than proton. Addition of methyl iodide before acid hydrolysis afforded **17**, **18**, and **19** in 13%, 45%, and 10% yields, respectively. All these products including even **17** might be formed via methylation of intermediate anion **15** which possesses three nucleophilic centers. Methylation on the nitrogen atom and on C(2) in the 1,3-oxathiane ring results in the formation of **17** and **18** via **20** and **21**, respectively. The intermediate ylide **22** formed by methylation at sulfur suffers hydrolysis and oxidation at some stage to give **19**.

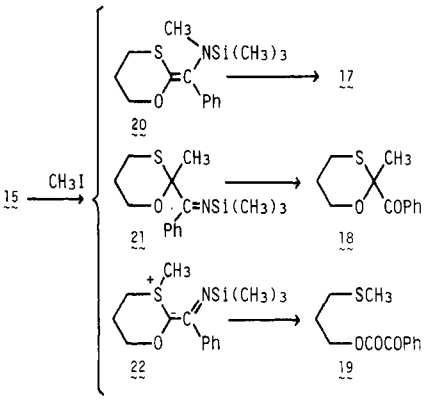
Discussion

The reaction of 2-heterosubstituted 1,3-oxathiane **23** and an anionic species Y^- is devided into three classes (Scheme III). In pathway i, Y^- acts as a base to pull off the proton at C(2) to give anion **24**. This type of reaction occurred in 2-silyl- and 2-germyl-1,3-oxathianes **1a** and **2a**. Pathway ii was recognized in the reaction of 2-(group 16)-substituted compounds. In 2-(methylseleno)-1,3-oxathiane (**8a**), pathway iii was competitive. Nucleophilic attack of Y^- on the heteroatom (pathway iii) was also observed in 2-stannyl and 2-plumbyl derivatives **3** and **4** to afford 1,3-oxathianyl anion **5a**. This type of metal–metal exchange reactions has been utilized to produce highly active anions such as an alkyl-substituted α-alkoxy organolithium[10] which could not be generated by the proton abstraction with bases.

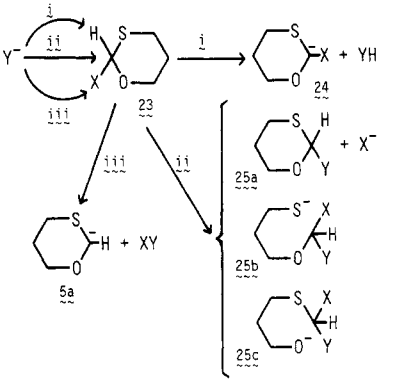
Scheme I



Scheme II



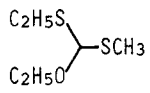
Scheme III



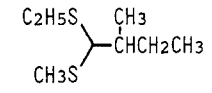
(1) Nucleophilic Displacement at C(2). Although pathway ii gives three possible products, **25a**, **25b**, and **25c**, depending upon the leaving group, attempted isolation of the compounds such as **25b** and **25c** from the reaction mixture of 2-(group 16)-substituted 1,3-oxathianes resulted in failure. In the open chain analogue **26** of 2-(methylthio)-1,3-oxathiane (**7a**), however, the third type of reaction involving an alkoxy group as a leaving group took place to afford **27** in 58% yield. The hard lithium cation coordinates with the oxygen atom which is harder than the sulfur atom so that the OR group becomes a better leaving group than the SR groups giving **27** as the major product. This accounts for the lower yield of **5c** from **7a** than from **6a**.

(2) 2-(Trimethylsilyl)-1,3-oxathianyl Anion (1b) as a Possible Acyl Dianion Equivalent. Utilization of acyl

(8) In this case 23% of deuterium was incorporated at C(2).
(9) Secker, J. A.; Thayer, J. S. *Inorg. Chem.* **1976**, *15*, 501.
(10) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481.



26



27

anion equivalents has become an important method of choice in synthetic organic chemistry. Especially, the usefullness of sulfur stabilized anions has been well documented.[11,12] However, the formation of an equivalent of the acyl dianion A by 1 molar equiv of base has never been described. Conversion of **1b** to 2-benzoyl-2-methyl-1,3-oxathiane (**18**) constitutes the generation of an acyl dianion equivalent A, provided that **18** is successfully converted to the parent carbonyl compound **28**. After a number of unsuccessful attempts,[13] we have found that **18** has been easily deblocked with nitryl iodide[14] to give 1-phenylpropane-1,2-dione (**28**) in 83% yield. Thus, 2-(trimethylsilyl)-1,3-oxathianyl anion (**1b**) can be regarded as an equivalent of the acyl dianion **A**.

Two successful chemical reactions, the alkylation or the acylation of a given anion and the successive conversion of the product to a parent carbonyl compound, are required for a given compound to be an acyl anion equivalent of synthetic utility. To meet these requirements it is necessary to increase the yield of **18**. Nevertheless, this sequence of reactions involving one-pot acylation–alkylation could provide a possible synthetic method for other 1,2-diketones.

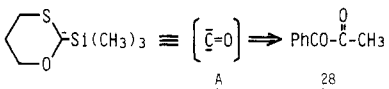
Experimental Section

Melting points were determined with a Yanagimoto micro apparatus and uncorrected. Infrared spectra were recorded with a JASCO A-202 diffraction grating infrared spectrometer. ^{1}H NMR spectra were obtained with a JEOL JNM-FX100 spectrometer. Chemical shifts are given as δ values relative to internal tetramethylsilane. Mass spectra were determined on a JEOL Model JMS-01SG double-focusing mass spectrometer. GLC analyses were performed on a Shimadu GC-4CM gas chromatograph. Prepative GLC was performed on a Varian aerograph Model 920 with a thermal conductive detector. All reactions involving organolithium reagents were carried out in an atmosphere of dry nitrogen. THF was predistilled with NaOH and freshly distilled from sodium benzophenone ketyl. *sec*-BuLi was prepared by the procedure of Gilman.[16]

Materials. Preparation of 2-heterosubstituted 1,3-oxathianes **1a**, **2a**, **3**, **4**, **6a**, **7a**, **8a**, and **9** was reported in the preceeding paper.

2-(Dimethylthiophosphinoyl)-1,3-oxathiane (10a). To a solution of 2-lithio-1,3-oxathiane (**5a**) prepared from 267 mg (2.56 mmol) of 1,3-oxathiane in 5 mL of THF was added 363 mg (2.82 mmol) of dimethylthiophosphonyl chloride[17] in 5 mL of THF, and stirred at −78 °C for 1.5 h. The reaction temperature was gradually raised to room temperature over 24 h. The reaction mixture was poured into ice–water, extracted with ether, dried ($MgSO_4$), filtered, and evaporated to leave a crude residue, which was purified by distillation to afford 88 mg (18%) of **10a**, bp 136–146 °C (0.5 mmHg). Repurification by GLC (2.5% Versamide) gave an analytical sample: mp 108–109.5 °C; IR ($CHCl_3$) 1065, 910 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.44–2.27 (m, 2 H), 1.79 (d, 3 H, J = 13 Hz), 1.81 (d, 3 H, J = 13 Hz), 2.66–3.28 (m, 2 H), 3.69 (d, t, 1 H, J = 4, 12 Hz), 4.25 (bd, 1 H, J = 12 Hz), 5.25 (d, 1 H, J = 4.2 Hz). Anal. Calcd for $C_6H_{13}OS_2P$: C, 36.72; H, 6.68. Found: C, 36.79; H, 6.94.

Scheme IV



1b

Preparation of 2-Deuterio-2-(trimethylsilyl)-1,3-oxathiane (1c). To a stirred solution of 51 mg (0.29 mmol) of 2-(trimethylsilyl)-1,3-oxathiane in 3 mL of THF was added a hexane solution of *sec*-BuLi at −78 °C until the solution was colored faint yellow. Nearly quantitative formation of **1b** in this solution was confirmed as follows: After stirring for a few minutes at −78 °C, deuterium oxide was added via a syringe. The reaction mixture was warmed up to 0 °C, poured into brine, and extracted with dichloromethane. The organic layer was dried (Na_2SO_4), filtered, and concentrated evaporatively to yield a crude oil. GLC analysis (10% FFAP) with 3,4-dimethylanisole as an internal standard indicated 79% recovery of the starting material. The crude material was purified by preparative GLC (10% FFAP). Integration of the proton at C(2) in the ^{1}H NMR spectrum of the purified material vs. any other well-defined and separated peaks of 2-(trimethylsilyl)-1,3-oxathiane indicated nearly quantitative incorporation of deuterium at C(2).

2-(Trimethylgermyl)-1,3-oxathiane (**2a**) afforded the corresponding deuterio derivative **2c** through essentially the same procedure including the purification process.

2-Deuterio-1,3-oxathiane (5b). To a 0.55-mmol solution of **3** or **4** in 4 mL of THF was added a hexane solution of *sec*-BuLi at −78 °C until the solution was colored faint yellow. After stirring for a few minutes at −78 °C deuterium oxide was added via a syringe. The mixture was warmed to 0 °C. The usual workup gave a crude oil. GLC analysis (10% FFAP) with β-methylnaphthalene as an internal standard indicated that more than 95% of 2-deuterio-1,3-oxathiane (**5b**) was obtained from **3** or **4**. Deuterium incorporation in each case was determined to be ~ 100% by ^{1}H NMR analysis.

Preparation of 2-*sec*-Butyl-1,3-oxathiane (5c). General Procedure. To a stirred solution of 24 mg (0.18 mmol) of 2-methoxy-1,3-oxathiane (**6a**) in 3 mL of THF was added a hexane solution of *sec*-BuLi at −78 °C until the solution was colored faint yellow. After the solution was stirred for 15 min at −78 °C, deuterium oxide was added via a syringe. The extractive workup gave a crude oil. GLC analysis (10% FFAP) with β-methylnaphthalene as an internal standard indicated a 57% yield of 2-*sec*-butyl-1,3-oxathiane (**5c**). The crude material was purified by preparative GLC (10% FFAP): colorless oil; IR ($CHCl_3$) 1460, 1075 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.6–2.2 (m, 11 H), 2.76 (bd, 1 H, J = 12 Hz), 3.00 (d, t, 1 H, J = 3.5, 12 Hz), 3.58 (d, t, 1 H, J = 3.5, 12 Hz), 4.14 (bd, 1 H, J = 12 Hz), 4.63 (d, 1 H, J = 6 Hz). Anal. Calcd for $C_8H_{16}OS$: C, 59.95; H, 10.06. Found: C, 59.88; H, 10.34.

Preparation of 2-Methyl-2-(trimethylsilyl)-1,3-oxathiane (1d). General Procedure. To a stirred solution of 2-lithio-2-(trimethylsilyl)-1,3-oxathiane (**1b**) prepared from 43 mg (0.24 mmol) of 2-(trimethylsilyl)-1,3-oxathiane (**1a**) was added methyl iodide (39 mg, 0.27 mmol) followed by stirring at −78 °C for 1.5 h. The yield of 2-methyl-2-(trimethylsilyl)-1,3-oxathiane (**1d**) was determined by GLC analysis (10% FFAP) with *p*-methylanisole as an internal standard. Extractive workup with diethyl ether and purification by preparative GLC (10% FFAP) gave pure **1d**, as a colorless oil: IR ($CHCl_3$) 1245, 1060, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.12 (s, 9 H), 1.56–2.20 (m, 2 H), 1.68 (s, 3 H), 2.56 (bd, 1 H, J = 13 Hz), 3.12 (d, d, d, 1 H, J = 4, 12, 13 Hz), 3.66 (bd, 1 H, J = 12 Hz), 3.92 (d, t, 1 H, J = 4, 12 Hz). Anal. Calcd for $C_8H_{18}OSSi$: C, 50.47; H, 9.53. Found: C, 50.57; H, 9.92.

1e: purified by preparative GLC (10% FFAP); colorless oil; IR ($CHCl_3$) 1245, 1065, 1005, 845 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.15 (s, 9 H), 0.98 (t, 3 H, J = 7 Hz), 1.48–2.08 (m, 2 H), 2.14 (q, 2 H, J = 7 Hz), 2.56 (bd, 1 H, J = 13 Hz), 3.04 (d, d, d, 1 H, J = 4, 12, 13 Hz), 3.68 (bd, 1 H, J = 12 Hz), 3.88 (d, t, 1 H, J = 4, 12 Hz). Anal. Calcd for $C_9H_{20}OSSi$: C, 52.89; H, 9.86. Found: C, 53.25; H, 9.85.

(11) Gröbel, B.-T.; Seebach, D. *Synthesis* **1977**, 357.
(12) Hase, T. A.; Koskimies, J. K. *Aldrichimica Acta* **1981**, *14*, 73.
(13) Though a large number of reagents have been developed for deblocking dithio or monothio acetals,[10] their application to those that have a carbonyl group at the α-position is limited because of destabilization of an intermediate onium ion.
(14) To our knowledge, nitryl iodide (INO_2) has never been applied for deblocking of dithio or monothiol acetals, though it has been used for other reactions.[15]
(15) Cherlrek, I.; Jewell, J. S.; Ritchie, R. G. S.; Szarek, W. A.; Jones, J. K. N. *Carbohydr. Res.* **1972**, *22*, 163 and the references cited therein.
(16) Gilman, H.; Moore, F. W.; Baine, O. *J. Am. Chem. Soc.* **1941**, *63*, 2479.
(17) Maier, L. *Chem. Ber.* **1961**, *94*, 3051.

1f: purified by preparative GLC (5% FFAP); colorless oil; IR ($CHCl_3$), 1245, 1065, 1010, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.18 (s, 9 H), 1.04 (d, 3 H, J = 7 Hz), 1.12 (d, 3 H, J = 7 Hz), 1.44–2.16 (m, 2 H), 2.52 (bd, 1 H, J = 14 Hz), 2.76 (q, 1 H, J = 7 Hz), 3.06 (d, d, d, 1 H, J = 4, 12, 14 Hz), 3.64 (bd, 1 H, J = 12 Hz), 3.77 (d, t, 1 H, J = 4, 12 Hz). Anal. Calcd for $C_{10}H_{22}OSSi$: C, 54.99; H, 10.15. Found: C, 55.27; H, 10.44.

1g: purified by preparative GLC (5% FFAP); colorless oil; IR ($CHCl_3$), 1245, 1060, 1005, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.18 (s, 9 H), 0.98 (d, 6 H, J = 6 Hz), 1.52–2.20 (m, 5 H), 2.48–3.12 (m, 2 H), 3.44–3.76 (m, 1 H), 3.76–4.12 (m, 1 H). Anal. Calcd for $C_{11}H_{24}OSSi$: C, 56.84; H, 10.41. Found: C, 56.86; H, 10.68.

1h: purified by preparative GLC (5% FFAP); colorless oil; IR ($CHCl_3$), 1245, 1065, 1020, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.19 (s, 9 H), 1.59–2.26 (m, 2 H), 1.99 (s, 3 H), 2.49 (bd, 1 H, J = 13 Hz), 3.30–3.80 (m, 2 H), 4.24 (d, t, 1 H, J = 3, 12 Hz). Anal. Calcd for $C_8H_{18}OS_2Si$: C, 43.20; H, 8.16. Found: C, 42.81; H, 8.49.

1i. The major isomer (the more polar spot) and the minor isomer (the less polar spot) were separated by preparative TLC (SiO_2). Major isomer: mp 107–108 °C (CH_2Cl_2 – hexane); IR ($CHCl_3$) 3550, 1240, 1005, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ –0.12 (s, 9 H), 1.40–2.12 (m, 3 H), 2.60 (bd, 1 H, J = 13 Hz), 3.14 (d, t, 1 H, J = 4, 13 Hz), 3.52–4.28 (m, 2 H), 5.46 (s, 1 H), 7.12–7.76 (m, 5 H). Anal. Calcd for $C_{14}H_{22}O_2SSi$: C, 59.53; H, 7.85. Found: C, 59.35; H, 8.01. Minor isomer: mp 107–108 °C (CH_2Cl_2–hexane); IR ($CHCl_3$) 3450, 1245, 1055, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ –0.14 (s, 9 H), 1.56–2.10 (m, 2 H), 2.60 (bd, 1 H, J = 13 Hz), 3.12 (d, t, t, 1 H, J = 4, 12, 13 Hz), 3.89 (bd, 1 H, J = 12 Hz), 4.29 (d, t, 1 H, J = 4, 12 Hz), 5.38 (s, 1 H), 7.16–7.61 (m, 5 H).

1j. The major isomer (the more polar spot) and the minor isomer (the less polar spot) were separated by preparative TLC (SiO_2). The major isomer was extremely unstable: IR ($CHCl_3$) 3560, 1240, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.12 (s, 9 H), 1.56–2.16 (m, 2 H), 2.24–2.80 (m, 2 H), 2.96–3.32 (m, 1 H), 3.60–4.16 (m, 2 H), 5.12 (d, d, 1 H, J = 2, 4 Hz), 6.44 (d, d, 1 H, J = 4, 16 Hz), 6.84 (d, d, 1 H, J = 2, 16 Hz), 7.20–7.60 (m, 5 H). Minor isomer: mp 114.5–115.5 °C (from CH_3CN); IR ($CHCl_3$) 3500, 1245, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.16 (s, 9 H), 1.44–2.24 (m, 2 H), 2.40–2.88 (m, 2 H), 2.96–3.36 (m, 1 H), 3.60–4.32 (m, 2 H), 5.02 (d, d, 1 H, J = 2, 4 Hz), 6.44 (d, d, 1 H, J = 4, 16 Hz), 6.76 (d, d, 1 H, J = 2, 16 Hz), 7.12–7.48 (m, 5 H). Anal. Calcd for $C_{16}H_{24}O_2SSi$: C, 62.29; H, 7.84. Found: C, 61.78; H, 7.87.

1k: mp 90.5–92.5 °C (ether–hexane); IR ($CHCl_3$) 3500, 1240, 1025, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ –0.08 (s, 9 H), 1.32–2.04 (m, 3 H), 2.04–2.40 (m, 1 H), 3.48–3.88 (m, 2 H), 4.00 (s, 1 H), 7.08–7.40 (m, 6 H), 7.72–8.04 (m, 4 H). Anal. Calcd for $C_{20}H_{26}O_2SSi$: C, 66.99; H, 7.31. Found: C, 66.72; H, 7.48.

11a: separated from a mixture involving **1k** by preparative TLC (SiO_2); colorless oil; IR ($CHCl_3$) 1732, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (t, 1 H, J = 8 Hz), 1.92 (quintet, J = 7 Hz, 2 H), 2.48 (q, 2 H, J = 7 Hz), 4.27 (t, 2 H, J = 7 Hz), 5.02 (s, 1 H), 7.30 (s, 10 H). Anal. Calcd for $C_{17}H_{18}O_2S$: C, 71.30; H, 6.33. Found: C, 71.56; H, 6.42.

12: 66% yield; mp 77–78.5 °C (from moist hexane); IR ($CHCl_3$) 3550, 1240, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.18 (s, 9 H), 1.08–2.04 (m, 12 H), 2.26 (s, 1 H), 2.60 (bd, 1 H, J = 12 Hz), 3.12 (d, t, 1 H, J = 4, 12 Hz), 3.68 (bd, 1 H, J = 12 Hz), 4.16 (d, t, 1 H, J = 4, 12 Hz). Anal. Calcd for $C_{13}H_{26}O_2SSi$: C, 56.88; H, 9.55. Found: C, 56.55; H, 9.70.

Preparation of 11b. To a stirred solution of 2-lithio-2-(trimethylsilyl)-1,3-oxathiane (**1b**) (1.0 mmol) was added 107 mg (1.1 mmol) of cyclohexanone via a syringe and the mixture stirred at –78 °C for 2 h. After warming to room temperature the reaction mixture was stirred for 15 h. The usual workup gave a crude product, which was purified by preparative TLC (SiO_2) affording 133 mg (66%) of **11b** as a colorless oil: IR ($CHCl_3$) 1720, 1165 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00–2.08 (m, 12 H), 2.08–2.44 (m, 1 H), 2.60 (q, 2 H, J = 7 Hz), 4.18 (t, 2 H, J = 7 Hz). Anal. Calcd for $C_{10}H_{18}O_2S$: C, 59.37; H, 8.97. Found: C, 59.71; H, 9.11.

Preparation of 2-Benzoyl-1,3-oxathiane (17). To a solution of 48 mg (0.27 mmol) of 2-(trimethylsilyl)-1,3-oxathiane (**1a**) was added *sec*-BuLi at –78 °C. After the reaction stirred for a few minutes, 42 mg (0.41 mmol) of benzonitrile was added via a syringe and stirring continued at –78 °C for 4 h. The mixture was poured into ice–water, acidified with 10% H_2SO_4, extracted with ether, dried ($MgSO_4$), filtered, and concentrated to leave a crude oil. Purification by SiO_2 preparative thin layer plate gave 42 mg (73%) of **17**, whose spectral data were identical with those of the standard.[1]

Reaction of 2-(Trimethylsilyl)-1,3-oxathiane with Benzonitrile Followed by Methyl Iodide. Preparation of 17, 18, and 19. To a stirred solution of 2-lithio-2-(trimethylsilyl)-1,3-oxathiane (**1b**) prepared from 101 mg (0.57 mmol) of **1a** was added 89 mg (0.86 mmol) of benzonitrile and the reaction stirred at –78 °C for 3.5 h. Then, 123 mg (0.87 mmol) of methyl iodide was added at –78 °C followed by stirring for 3.5 h at –78 °C. The mixture was poured into ice–water, acidified with 10% H_2SO_4, extracted with diethyl ether, dried ($MgSO_4$), filtered, and concentrated in vacuo to leave a crude oil. Purification by 0.5 mm SiO_2 plates gave 16 mg (13%) of **17**[1] and 57 mg (45%) of **18**: colorless oil; IR ($CHCl_3$) 1680, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.85 (3 H, s), 1.70–2.30 (m, 2 H), 2.76 (bd, 1 H, J = 13 Hz), 3.02 (d, t, 1 H, J = 4, 13 Hz), 3.76 (d, t, 1 H, J = 4, 13 Hz), 3.97 (bd, 1 H, J = 13 Hz), 7.20–7.68 (m, 3 H), 8.00–8.32 (m, 2 H). Anal. Calcd for $C_{12}H_{14}O_2S$: C, 64.84; H, 6.35. Found: C, 65.06; H, 6.50. Also, 14 mg (10%) of **19** was obtained: colorless oil; IR ($CHCl_3$) 1730, 1685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.80–2.24 (m, 2 H), 2.12 (s, 3 H), 2.64 (t, 2 H, J = 7 Hz), 4.51 (t, 2 H, J = 6 Hz), 7.34–8.16 (m, 5 H).

Preparation of 26. To a solution of 2.50 g (40.24 mmol) of ethanethiol in 20 mL of anhydrous ether was added 25.9 mL (40.15 mmol) of *n*-BuLi at –78 °C, to which a solution of 3.80 g (40.19 mmol) of chloromethyl ethyl ether in 5 mL of anhydrous ether was added at –78 °C and stirred for 3 h at –78 °C. The reaction mixture was directly distilled to give 4.18 g (87%) of 1-ethoxy-1-(ethylthio)methane: bp 136–138 °C; IR ($CHCl_3$) 1260, 1075, 1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (t, 3 H, J = 7 Hz), 1.33 (t, 3 H, J = 7.5 Hz), 2.65 (q, 2 H, J = 7.5 Hz), 3.60 (q, 2 H, J = 7 Hz), 4.70 (s, 2 H). Anal. Calcd for $C_5H_{12}OS$: C, 49.96; H, 10.06. Found: C, 49.76; H, 10.49.

To a solution of 960 mg (7.99 mmol) of 1-ethoxy-1-(ethylthio)methane in 15 mL of THF was added *sec*-BuLi at –78 °C until the solution was colored faint yellow. After the solution was stirred for a few minutes at –78 °C, 1.13 g (12.0 mmol) of dimethyl disulfide was added and the mixture stirred at –78 °C for 2 h. The usual workup gave **26** as a crude oil [856 mg, 65% by GLC (5% FFAP) with *p*-methylanisole as an internal standard], which was purified by distillation: bp 100–103 °C (16 mmHg); IR ($CHCl_3$) 1360, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (t, 3 H, J = 7.0 Hz), 1.29 (t, 3 H, J = 7.5 Hz), 2.16 (s, 3 H), 2.68 (q, 1 H, J = 7.5 Hz), 2.69 (q, 1 H, J = 7.5 Hz), 3.70 (q, 1 H, J = 7.0 Hz), 3.71 (q, 1 H, J = 7.0 Hz), 5.66 (s, 1 H). Anal. Calcd for $C_6H_{14}OS_2$: C, 43.34; H, 8.49. Found: C, 42.85; H, 8.94.

Reaction of 26 with *sec*-BuLi. Preparation of 27. To a solution of 54 mg (0.32 mmol) of **26** in 5 mL of THF was added *sec*-BuLi until the solution was colored faint yellow. After the solution stirred for a few minutes, D_2O was added. The usual workup gave a crude oil. GLC analysis (10% FFAP) with *p*-methylanisole as an internal standard indicated 33.3 mg n58%) of **27**: IR ($CHCl_3$) 1210, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (t, 3 H, J = 7 Hz), 1.06 (d, 3 H, J = 7 Hz), 1.26 (t, 3 H, J = 7 Hz), 1.36 (q, 2 H, J = 7), 1.60–1.96 (m, 1 H), 2.15 (s, 3 H), 2.64 (q, 2 H, J = 7 Hz), 3.68 (d, 1 H, J = 5 Hz), spectral data were consistent with the assigned structure.[18]

3-(Methylthio)propyl Phenylglyoxylate (19). A mixture of thionyl chloride (950 mg, 8.0 mmol) and phenylglyoxylic acid (1.0 g, 6.7 mmol) was stirred at 40 °C overnight. Evaporation in vacuo below 20 °C to leave a crude oil, to which 200 mg (0.9 mmol) of 3-(methylthio)propanol was added at 0 °C and the mixture stirred for 7 h at 0 °C. The mixture was poured into ice–water, extracted with dichloromethane, washed with water, dried ($MgSO_4$), and evaporated to leave a crude oil. It was purified by SiO_2 column chromatography to give a 81% yield of **19** as a colorless oil, whose IR and ^1H NMR spectra were identical with those of the product **19** from the reaction of **1a** and cyanobenzene.

1-Phenylpropane-1,2-dione (28). To a stirred solution of 154 mg (0.61 mmol) of I_2 and 94 mg (0.61 mmol) of $AgNO_2$ in 4 mL of ether was added a solution of 123 mg (0.55 mmol) of **18** in aqueous ether (4 mL), and the solution stirred at room temper-

(18) Neither a satisfactory combusion analysis nor a molecular ion in the mass spectrum was obtained because of instability of the product.

ature for 5.5 h. The mixture was poured into an ice-$Na_2S_2O_3$ solution, extracted with ether, dried ($MgSO_4$), filtered, and evaporated to leave a crude oil. It was purified by 0.5-mm SiO_2 plates to give 68 mg (83%) of **28** as a yellow oil: IR ($CHCl_3$) 1715, 1675, 1600, 1165, 905 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.53 (s, 3 H), 7.25-7.70 (m, 3 H), 7.86-8.23 (m, 2 H). Spectral data were identical with those of an authentic specimen.[19]

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(20) The group notation is being changed in accord with recent actions by IUPAC and ACS nomenclature committees. A and B notation is being eliminated because of wide confusion. Group I becomes groups 1 and 11, group II becomes groups 2 and 12, group III becomes groups 3 and 13, etc.

Registry No. **1a**, 79143-99-0; **1b**, 86137-19-1; **1c**, 79144-08-4; **1d**, 94620-84-5; **1e**, 94620-85-6; **1f**, 94620-86-7; **1g**, 94620-87-8; **1h**, 94620-88-9; (*R**,*R**)-**1i**, 94620-89-0; (*R**,*S**)-**1i**, 94620-90-3; (*R**,*R**)-**1j**, 94620-91-4; (*R**,*S**)-**1j**, 94620-92-5; **1k**, 94620-93-6; **2a**, 79144-00-6; **2c**, 79144-09-5; **3**, 79144-01-7; **4**, 79144-02-8; **5a**, 64554-58-1; **5b**, 79144-10-8; (*R**,*R**)-**5c**, 94620-81-2; (*R**,*S**)-**5c**, 94620-99-2; **6a**, 79144-05-1; **10a**, 94620-82-3; **10c**, 94620-83-4; **11a**, 94620-94-7; **11b**, 94620-96-9; **12**, 94620-95-8; **17**, 86137-20-4; **18**, 86137-22-6; **19**, 86137-21-5; **26**, 94620-97-0; **27**, 94620-98-1; **28**, 579-07-7; *sec*-BuLi, 598-30-1; MeI, 74-88-4; EtI, 75-03-6; *i*-PrI, 75-30-9; *i*-BuI, 513-38-2; $(MeS)_2$, 624-92-0; PhCHO, 100-52-7; PhCH=CHCHO, 104-55-2; PhCOPh, 119-61-9; $ClP(S)Me_2$, 993-12-4; PhCN, 100-47-0; C_2H_5SH, 75-08-1; $C_2H_5OCH_2Cl$, 3188-13-4; $C_2H_5SCH_2OC_2H_5$, 54699-20-6; $PhCOCO_2H$, 611-73-4; $CH_3S(CH_2)_3OH$, 505-10-2; cyclohexanone, 108-94-1.

Polyaza Cavity Shaped Molecules. 2. Annelated Derivatives of 2,2'-Biquinoline and the Corresponding *N*-Oxides

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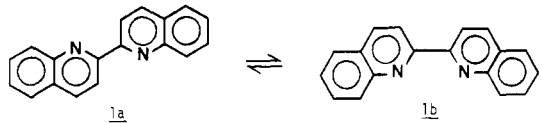
Received May 22, 1984

The reaction of *o*-aminobenzaldehyde with cyclic 1,2-diketones provided 3,3'-annelated derivatives of 2,2'-biquinoline. The reaction with 1,2-cyclododecanedione stopped at the monocondensation stage. High-resolution NMR spectra demonstrate that the dimethylene- and trimethylene-bridged systems are undergoing rapid conformational inversion at room temperature while the tetramethylene-bridged system is conformationally rigid. The chemical shift of the H-8 proton is found to be closely related to the biquinoline dihedral angle. Mono- and di-*N*-oxides were prepared by reaction of annelated biquinolines with *m*-chloroperbenzoic acid. The di-*N*-oxide of the trimethylene-bridged system was found to be conformationally rigid by NMR.

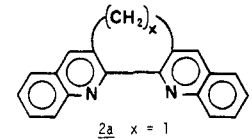
The 2,2'-biquinoline molecule can be considered as a dibenzo derivative of 2,2'-bipyridine. It may exist in two planar conformations: anti (**1a**) and syn (**1b**). An X-ray



1a **1b**

determination has revealed that the anti form is preferred in the solid state.[1] It is the syn form, however, through which bidentate chelation can occur. As has been pointed out by earlier workers,[2,3] the fused benzo rings serve to sterically congest the coordinating pocket of the molecule in its syn conformation and limit the types of complexation which can occur.

We have prepared a series of 3,3'-annelated 2,2'-biquinolines **2** in which the length of the annelating bridge controls the relative orientation of the two rings and thus influences the shape of the chelating "bite" as well as other types of cooperative chemistry which the two nitrogens might undergo. In this paper we discuss the preparation of the annelated biquinolines **2a-d**, a spectroscopic investigation of their conformational properties, and the preparation and characterization of mono- and di-*N*-oxide derivatives.



2a x = 1
b x = 2
c x = 3
d x = 4

Synthesis. The reaction of *o*-acetyl- or *o*-benzoylaniline with cyclic α-diketones has been utilized to prepare 4,4'-disubstituted derivatives of **2a-c**.[4] It has also been demonstrated that *o*-aminobenzaldehyde will condense with 1,2-cyclohexanedione to provide **2b**.[5] We have applied this same reaction to a series of cyclic α-diketones ranging from 5 to 12 carbons in ring size. For rings up to eight carbons, the condensation occurs smoothly to provide **2a-d** in good yields. Previously we have reported that this same type of condensation may be carried out with 2-aminonicotinaldehyde to provide 3,3'-annelated 2,2'-bi[1,8]-naphthyridines.[6] The reaction of *o*-aminobenzaldehyde with 1,2-cyclododecanedione occurs at only one carbonyl group such that the monocondensation product **5** is formed exclusively. In an independent study we are investigating

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