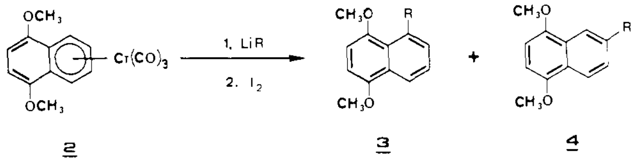
Table I. Reactions of Carbanions with Complex **2**



entry	carbanion LiR	time, h/ temp, °C	product mixture[a] ratio, % 3	4	combined yield,[b] %
1	$LiCH_2CN$	1/−50	75[c]	25[c]	34[c]
2	$LiCH_2CN$	30/−20	100	0	72
3	$LiC(CH_3)_2CN$	0.5/−60	22	78	69
4	$LiC(CH_3)_2CN$	1/−40	27	73	84
5	$LiC(CH_3)_2CN$	2/0	47	53	76
6	$LiC(CH_3)_2CN$	46/0	97[c]	3[c]	72[c]
7	$LiCH_2COO$-*t*-Bu	1/0	67	33	89
8	$LiCH_2COO$-*t*-Bu	48/0	>98[c]	<2[c]	84[c]
9	$LiC(CH_3)S(CH_2)_3S$	1/0	0	100	61
10	$LiC(CH_3)S(CH_2)_3S$	48/0	0	100	71

[a] All compounds were isolated and independently characterized. Their IR, ^1H NMR (360 MHz), and mass spectra are in full agreement with the assigned structures. The product ratios are based on isolated material (unless otherwise noted). [b] The percentage yields refer to isolated (column chromatography) material after separation into 3 and 4 (unless otherwise indicated). [c] Ratio determined by ^1H NMR integration, combined yields refer to mixtures of 3 and 4.

considered extremely slow below 0 °C.[18] Furthermore, product distributions resulting from reactions with substituted-benzene complexes were reported to be invariant to changes in reaction time and temperature (0.5 min at −78 °C to 24 h at 25 °C), strongly suggesting kinetic control of the reaction.[2] In contrast, in reactions of **2** reversibility of the addition to the kinetically favored intermediate depends largely on the nature of the anion. Irreversible β addition is only observed with 2-lithio-2-methyl-1,3-dithiane (entries 9 and 10). The different behavior of the sulfur-stabilized carbanion compared to the ester enolate (entries 7 and 8) and the cyano-stabilized carbanions (entries 1–6) may simply reflect the difference in the pK_a value of the conjugate acid.

The regiospecific β attack of methyldithiane anion can be interpreted in terms of steric and electron-pair repulsion between the incoming anion and the methoxy group. In a synthetic application this reaction provides the key step in a short and novel route to the daunomycinone precursor 1,4-dimethoxy-6-acetyltetralin (**6**)[19] (Scheme I).

Starting with 1,4-dimethoxynaphthalene, regiospecific[16] introduction of the $Cr(CO)_3$ group was achieved in 91% yield by a procedure described previously.[11] Reaction of **2** with 2-lithio-2-methyl-1,3-dithiane in THF/HMPT followed by protonation[20] of the intermediate and decomplexation (Ce(IV)) resulted in nucleophilic addition of the masked-carbonyl function with reduction of one double bond to yield, after chromatography on silica gel and crystallization (ether/hexane), the dihydronaphthalene **5** (mp 102 °C, 62%). Dithiane hydrolysis followed by hydrogenation yielded a 5:1 mixture of the desired product **6** and its aromatic counterpart (78% yield).

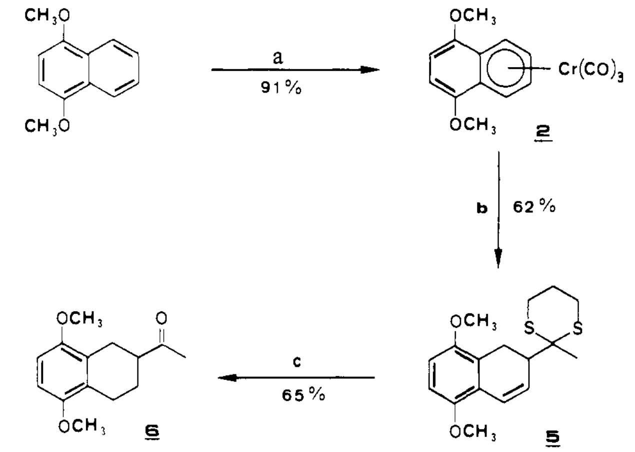
In summary, the results presented indicate the delicate balance that exists among the factors affecting regioselectivity and reversibility of the addition of carbanions to complex **2**. Further

(18) Semmelhack, M. F.; Hall, H. T.; Jr.; Farina, R.; Yoshifuji, M.; Clark, G.; Bargar, T.; Hirotsu, K.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 3535–3544.

(19) Wong, C. M.; Popien, D.; Schwenk, R.; Te Raa, J. *Can. J. Chem.* **1971**, *49*, 2712–2718.

(20) In contrast to the cyclohexadienyl $Cr(CO)_3$ anions where protonation necessitates treatment with an excess of strong acid (e.g., CF_3COOH),[18] protonation of our intermediate occurs readily to yield, as the sole product, the desired isomer **5**. In general, protonation and oxidation steps were carried out in one operation with 3 equiv of Ce^{IV} in aqueous THF.

Scheme I[a]



[a] All reactions were carried out under nitrogen. Key: (a) Bu_2O/hexane (10/1), THF (1 mL), $Cr(CO)_6$, reflux 3 days; (b) (i) $LiC(CH_3)S(CH_2)_3S$, THF/HMPA (9/1), 0 °C, 60 h; (ii) $Ce(NH_4)_2(NO_3)_6$ (3 equiv), THF/H_2O (9:1), −78 °C → room temperature, 12 h; (c) (i) *N*-chlorosuccinimide (4 equiv), $AgNO_3$, collidine, 25 °C, 2 min, saturated aqueous Na_2SO_3, saturated aqueous $NaHCO_3$, CH_2Cl_2; (ii) H_2 (1 atm), Pd/C (10%), room temperature.

mechanistic and synthetic studies along these lines are in progress in our laboratory.

Acknowledgment. Financial support of this work by the Swiss National Science Foundation (Grant 2.318-0.81) is gratefully acknowledged.

Registry No. 2, 12111-66-9; **3** (R = CH_2CN), 87555-39-3; **3** (R = $C(CH_3)_2CN$), 87555-40-6; **3** (R = CH_2COO-*t*-Bu), 87555-41-7; **4** (R = CH_2CN), 87555-42-8; **4** (R = $C(CH_3)_2CN$), 87555-43-9; **4** (R = CH_2COO-*t*-Bu), 87555-44-0; **4** (R = $C(CH_3)S(CH_2)_3S$), 87555-45-1; **5**, 87566-96-9; **6**, 33654-68-1; $LiCH_2CN$, 20428-58-4; $LiC(CH_3)_2CN$, 50654-53-0; $LiCH_2COO$-*t*-Bu, 41850-36-6; $LiC(CH_3)S(CH_2)_3S$, 27969-97-7.

Aldol Reaction of Silyl Enol Ethers with Aldehydes under Neutral Conditions[1]

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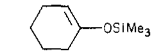
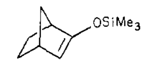
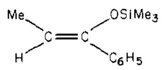
The aldol reaction, usually carried out with base or acid as the catalyst, is one of the most fundamental reactions in organic chemistry.[2] In recent years, the development of new methods for the directed aldol reaction has seen rapid growth in relation to control of acyclic stereochemistry.[2a,3] Several important un-

(1) Organometallic High-Pressure Reaction. 2. Part 1: Yamamoto, Y.; Maruyama, K.; Matsumoto, K. *J. Chem. Soc., Chem. Commun.* **1983**, 489.

(2) (a) Mikaiyama, T. *Org. React.* **1982**, *28*, 203; (b) "Carbon–Carbon Bond Formation"; Augustine, R. L., Ed.; Marcel Dekker: New York, 1979; Vol. 1.

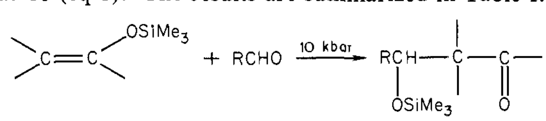
(3) (a) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, 13, 1. (b) Heathcock, C. H. *Science (Washington, D.C.)* **1981**, *214*, 395. (c) Masamune, S.; Choy, W. *Aldrichim. Acta* **1982**, *15*, 47. (d) Bartlett, P. D. *Tetrahedron*, **1980**, *36*, 3.

Table I. Reaction of Silyl Enol Ethers with Aldehydes under High Pressure[a]

entry	silyl enol ether	aldehyde	condition: temp, °C, day	erythro/threo[b] (with $TiCl_4$)[c]	total yield, %[b]
1	 (2)	C_6H_5CHO[d]	50–60, 9	75/25 (25/75)[e]	90
2	2	$p\text{-}O_2NC_6H_4CHO$	room temperature, 9	75/25 (25/75)	20
3	2	$p\text{-}MeOC_6H_4CHO$	50–60, 7	53/47	42
4	 (3)	C_6H_5CHO	room temperature, 9	44/56 (42/58)	41
5	3	C_6H_5CHO	50–60, 5	44/56	75
6	3	$p\text{-}O_2NC_6H_4CHO$	room temperature, 7	11/89 (46/54)	20
7	3	$p\text{-}O_2NC_6H_4CHO$	50–60, 7	11/89	83
8	3	$p\text{-}MeOC_6H_4CHO$	50–60, 5	45/55	82
9	 (4)	C_6H_5CHO	50–60, 6	25/75 (58/42)	25
10	4	$p\text{-}O_2NC_6H_4CHO$	room temperature, 6	28/72	30
11	4	$p\text{-}MeOC_6H_4CHO$	50–60, 7	46/54	35

[a] In a Teflon capsule (1.5-mL capacity) were placed the aldehyde (1 mmol), the silyl enol ether (1 mmol), and solvent (ca. 1 mL, normally CH_2Cl_2). High-pressure (10 kbar) experiments were performed in a stainless steel die and compressed via a piston. [b] By ^1H NMR spectroscopy of 1 and the hydrolysis product. [c] Erythro/threo under the condition of the Mukaiyama reaction using $TiCl_4$. [d] Ethyl ether was used as solvent. [e] The data of ref 4a.

answered questions remain concerning the Mukaiyama reaction.[4] What is the role of $TiCl_4$? Does $TiCl_4$ act only as the activator of carbonyl groups or does the reaction proceed through the corresponding titanium enolate?[5] What is the stereochemistry in the absence of Lewis acid? To help clarify these problems and to get better insight into the genuine aldol reaction, we have examined the reaction of silyl enol ethers with aldehydes under neutral conditions by using a high-pressure technique (10 kbar). To our surprise the aldol reaction occurred even at room temperature (eq 1). The results are summarized in Table I.



(1)

1

The reaction is generally very clean and no side reactions are accompanied. When the reaction is incomplete, the starting materials are recovered without change. The adduct (**1**) is hydrolyzed to give the corresponding aldol. Heating at 50–60 °C accelerates the reaction and the results of entries 4–7 indicate that the adduct does not isomerize under the reaction condition. Further, this was confirmed by the control experiment using a mixture of threo and erythro isomers of **1** derived from **2** and benzaldehyde. Interestingly, the stereoselectivity is significantly dependent upon the substituent of phenyl group. More importantly, however, *the stereoselectivity of **2** and **4** reverses in comparison with that of the Mukaiyama reaction.* With $TiCl_4$, **2** gives the threo isomer predominantly (entries 1 and 2) and **4** affords the erythro isomer with slight preference (entry 9). These results are in agreement with prediction from a cyclic chair transition state.[4b,c]

The erythro selectivity of **2** can be explained by the steric effect arising from S_E-type attack by carbonyl electrophiles to the β-carbon of **2**, as we previously proposed.[6] We next examined the reaction of α-mercuriopropiophenone with benzaldehyde in the presence of $BF_3{\cdot}OEt_2$. Fortunately, the ratio of erythro/threo was 28/72.[7] Consequently, the selectivity of **2** and **4** is analogous to the selectivity via the S_E-type reaction.[8] To obtain further support to the S_E-type mechanism, the reaction of α-(trimethylsilyl)propiophenone[9] with benzaldehyde was examined under 8 kbar at room temperature. However, the starting materials were recovered. Therefore, the present unique stereoselectivity can not be ascribed to the S_E-type mechanism.

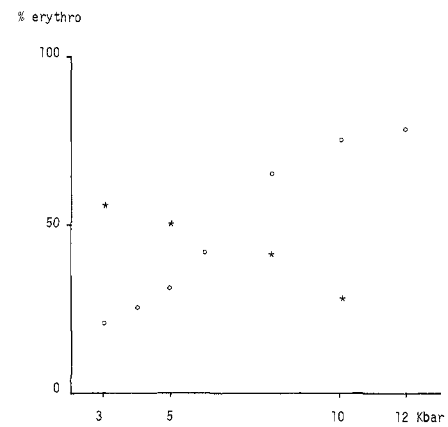


Figure 1. Pressure effect on diastereoselectivity. (○) Reaction of **2** with *p*-nitrobenzaldehyde; (☆) Reaction of **4** with *p*-nitrobenzaldehyde. The ratio of erythro to threo isomer was determined by HPLC analysis and/or ^1H NMR spectroscopy.

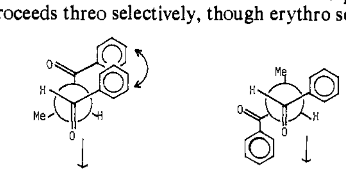
The erythro selectivity of **2** and the threo selectivity of **4** may be explained via a boat transition state. A boat-preferred transition state has not been considered for an ordinary enolate such as **2**

(4) (a) Mukaiyama, T.; Banno, K.; Narasaka, T. *J. Am. Chem. Soc.* **1974**, *96*, 7503. (b) Chan, T. H.; Aida, T.; Lau, P. W. K.; Gorys, V.; Harpp, D. N. *Tetrahedron Lett.* **1979**, 4029. (c) Yamamoto, K.; Tomo, Y.; Suzuki, S. *Chem. Lett.* **1980**, 2861.

(5) In the reaction of ketene silyl acetals in the presence of $TiCl_4$, titanium enolates are proposed: Inaba, S.; Ojima, I. *Tetrahedron Lett.* **1977**, 2009. Wallace, I. H. M.; Chan, T. H. *Tetrahedron* **1983**, *39*, 847. See also: Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1983**, 3347.

(6) Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1982**, *104*, 2323.

(7) It has been revealed that the reaction of α-mercuriopropiophenone with benzaldehyde proceeds threo selectively, though erythro selectivity is usually



exhibited with other α-mercurioketones.[6] The reason for this difference may be due to the steric repulsion between two phenyl groups.

(8) We also examined the reaction of α-mercurionorbornanone with benzaldehyde. However, the aldol reaction did not take place, presumably owing to the steric effect of norbornane structure. Whether $TiCl_4$ is present or not, **3** exhibits threo selectivity (entries 4–7). This threo-selectivity may also be due to the characteristic structural feature of norbornane moiety.

(9) The α-silyl ketone was prepared by the method of Matsuda: Matsuda, I.; Sato, S.; Izumi, Y. *Chem. Lett.* **1983**, 2787.

or **4**.[10] To check a possibility that high pressure induces a crossover from a chair-preferred to a boat-preferred transition state, the pressure effect on the stereoselectivity was examined at room temperature in the range 3–12 kbar. Although the conversion was low at low pressure, the erythro/threo ratio was obtained by HPLC analysis. The results are summarized in Figure 1. Quite interestingly, a remarkable pressure effect is observed. At low pressure (3–5 kbar), the reaction of **2** with nitrobenzaldehyde produces the threo isomer predominantly while **4** gives the erythro isomer with slight preference. Therefore, the stereoselectivity at low pressure is in agreement with a chair transition state. It is reasonable to assume that $\Delta V^{\neq}$ is different for both chair and boat transition states and a boat transition state is favored at high pressure because of its tight character.

In conclusion, (i) $TiCl_4$ plays an important role for controlling the stereoselectivity in the Mukaiyama reaction. As recognized in several recent papers,[11] here also, Lewis acid serves as a stereosteering group as well as an activator of carbonyl groups. (ii) High pressure creates the stereoselectivity via a boat transition state, while low pressure produces the stereoselectivity via a chair transition state.

(10) It is usually thought that enolates bearing a bulky group at the β-position, such as *tert*-butyl group, proceed through a boat-preferred transition state.[3a] See also: Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1983**, 3343.
(11) (a) Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7107. (b) Trost, B. M.; O'Krongly, D.; Belletire, J. L. *Ibid.* **1980**, *102*, 7595. (c) Danishefsky, S.; Kato, N.; Askin, D.; Kerwin, J. F., Jr. *Ibid.* **1982**, 104, 360. (d) Oppolzer, W.; Chapuis, C.; Dao, G. M.; Reichlin, O.; Godel, T. *Tetrahedron Lett.* **1982**, 4781. (e) Heathcock, C. H.; Flippin, L. A. *J. Am. Chem. Soc.* **1983**, *105*, 1667.

First Example of an Isolable σ-Sulfurane with an Apical Alkyl Group Effected by Transannular Bond Formation between the Amino and the Sulfonio Groups

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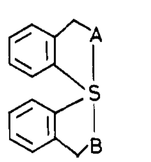
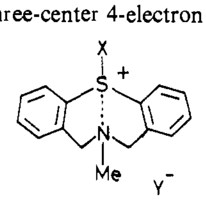
Whereas a variety of σ-sulfuranes of type **1** have been synthesized and the structures have been determined by X-ray crystallographic analysis,[1] every compound bears electron-withdrawing apical groups such as A and B due to the electron-rich and polarizable nature of the apical three-center 4-electron bond.[2]



1

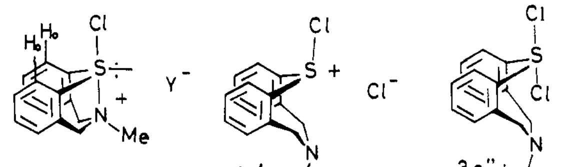


2, X = O^-
3a, X = Me
b, X = Et
c, X = MeO
d, X = EtO
e, X = Cl

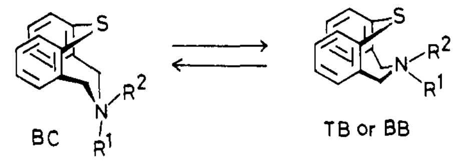
Hence there has been no example of an isolated σ-sulfurane with an electron-donating alkyl group at the apical position. Now we report the transannular bond formation between the amino and the sulfonio groups[3] of S-substituted *N*-methyl-6,7-dihydro-5*H*-dibenzo[*b*,*g*][1,5]thiazocinium salt (**3**), which afforded the first example of such σ-alkylsulfuranes as **3a** and **3b**, although σ-sulfurane with an equatorial methyl group was reported by Lau and Martin.[4]

Sulfoxide **2**[5] was converted to *S*-chloro chloride **3e-i** (Y = Cl) with excess thionyl chloride in benzene at room temperature quantitatively. Treatment of the suspension of the chloride with lithium dimethyl cuprate (1.2 equiv) in ether–THF at −78 °C furnished *S*-methyl hexafluorophosphate **3a** (Y = PF_6).[6] **3a** was converted to *S*-ethyl hexafluorophosphate **3b** (Y = PF_6) by reaction of methyl iodide with the intermediate sulfonium ylide, which was generated from **3a** with *n*-butyllithium in THF at −78 °C. **3e** was hydrolyzed with aqueous sodium carbonate to give back **2** quantitatively. **2** was alkylated with Meerwein reagent in dichloromethane to afford *S*-alkoxy hexachloroantimonates **3c** (Y = $SbCl_6$) and **3d** (Y = $SbCl_6$).

The reasonable structure of **3e** was assigned as σ-ammonio-*S*-chlorosulfurane, and not as **3e′** nor **3e″**, on the basis of the following facts:



3e 3e′-i 3e″-i



BC TB or BB

4, R^1 = alkyl; R^2 = lone pair electron
5 (ammonium salt), $R^1 = R^2$ = Me

(i) ^1H NMR spectrum of **3e-i** (Y = Cl) shows singlets at δ 3.13 (NMe) and at 4.65 (CH_2) in CD_3CN, and no change is observed when the chloride ion is exchanged for hexachloroantimonate (**3e-ii**, Y = $SbCl_6$) or hexafluorophosphate (**3e-iii**, Y = PF_6), (ii) the chemical shift of NMe of **3e** is close to that of the corresponding *N*,*N*-dimethylammonium sulfide (**5**: δ 3.16) of *TB* or *BB* form, (iii) aromatic ortho hydrogens of **3e** appear at lower field (δ 8.23–8.63, m, 2 H) than other aromatic hydrogens (δ 7.22–8.02, m, 6 H), probably due to the effect of the polarizable apical bond.[7]

S-Methyl (**3a**) and *S*-methoxy (**3c**) compounds also show one type of singlets for the NMe and the methylene groups, i.e., **3a** δ 2.53, 4.06 (in CD_3CN) and **3c** δ 2.77, 4.25. ^1H NMR spectra of **3a**, **3c**, and **3e** did not show any temperature dependence between 70 and −30 °C.

Conformational analyses of *N*-methyl-6,7-dihydro-5*H*-dibenzo[*b*,*g*][1,5]thiazocine (**4**) and related compounds were investigated in detail by Ollis et al., Leonard et al., and Mehta et al.[8] In equilibrium (**1**), the boat-chair (*BC*) conformation has

(1) (a) Kapovits, I.; Kalman, A. *J. Chem. Soc., Chem. Commun.* **1971**, 649. (b) Perozzi, E. F.; Martin, J. C. *J. Am. Chem. Soc.* **1972**, *94*, 5519. (c) Adzima, L. J.; Chiang, C. C.; Paul, I. C.; Martin, J. C. *Ibid.* **1978**, *100*, 953. (d) Kapovits, I.; Rabai, J.; Ruff, F.; Kucsman, A. *Tetrahedron* **1979**, *35*, 1869; *Ibid.* **1979**, *35*, 1875. (e) Perozzi, E. F.; Martin, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 1591. (f) Michalak, R. S.; Martin, J. C. *Ibid.* **1982**, *104*, 1683.
(2) Musher, J. I. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 54 and references cited therein.
(3) There has been no intended discussion on the interaction between the amino and the sulfonio groups, see: Ohara, Y.; Akiba, K.; Inamoto, N. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1508. The result of theoretical treatment of this bonding will be published elsewhere by K. Morokuma, M. Hanamura, and K. Akiba.
(4) Lau, P. H. W.; Martin, J. C. *J. Am. Chem. Soc.* **1977**, *99*, 5490.
(5) Tanaka, S.; Watanabe, H.; Ogata, Y. *Yakugaku Zasshi (Tokyo)* **1973**, *93*, 997.
(6) The reaction mixture was quenched with an aqueous solution of potassium hexafluorophosphate and ammonium chloride (5:1 by weight). Products (**3a–d**) were recrystallized from ether–acetonitrile.
(7) Astrologes, G. W.; Martin, J. C. *J. Am. Chem. Soc.* **1977**, *99*, 4390. Granoth, I.; Martin, J. C. *Ibid.* **1981**, *103*, 2711.

0002-7863/83/1505-6965$01.50/0