the low-temperature carbon-13 spectra of **4** in a 3:1 mixture of acetaldehyde and acetone.[15] At room temperature, chemical shifts relative to internal TMS of δ 159.06, 141.05, and 99.22 were found for the carbonyl carbon, the alkene carbon bonded to oxygen, and the CH_2 alkene carbon, respectively. Upon cooling, the first two carbons decoalesce, and chemical shifts at −110 °C of δ 159.51 and 163.58 were found for the carbonyl carbon and δ 140.23 and 145.07 for the alkene carbon attached to oxygen. The carbonyl carbons of the *E* conformations of alkyl[2,16] and aryl formates[7] have been found to absorb downfield of the *Z* conformations, and the minor (downfield) signals for both carbons of **4** were also assigned to the *E* isomer. From electronic integration, populations of 0.05 and 0.95 were found for the *E* and *Z* conformations, and populations at the coalescence temperature for the carbonyl group (−87 °C) were estimated with the assumption that $\Delta G°$ (0.95 kcal/mol) is independent of temperature. Rate constants of 620 and 47 s^{-1} were obtained[17] at −87 °C for the $E \rightarrow Z$ and $Z \rightarrow E$ conversions, and the corresponding barriers are $8.3_4 \pm 0.2$ and $9.2_9 \pm 0.2$ kcal/mol. These values are close to the barriers found for phenyl formate (8.1 and 8.5 kcal/mol).[7]

Molecular-orbital calculations for the *E* conformations indicate[11,12] that **4c** is more stable than **4d** and, as noted above, **4a** is lower in energy than **4b**. The conformational equilibrium can therefore be represented as **4a** ⇌ **4c**; any small amounts of **4b** or **4d** could not be detected separately in the slow-exchange carbon spectrum, as their signals would be averaged with **4a** or **4c**, respectively.

The estimate[12] that **4a** is at least 2.3 kcal/mol more stable than the next conformation is shown to be too high for solutions in a polar solvent. The finding of a larger population of (*E*)-vinyl formate (0.05) than for (*E*)-methyl formate (0.003)[2] provides evidence that aromaticity is an important effect in stabilizing the *Z* conformations of most esters.[18]

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(15) Spectra were recorded unlocked at 75.57 MHz, and the signal-to-noise ratio was improved by exponential multiplication of the FID, resulting in a line broadening of 3 Hz. A concentration of 20% by volume was used. Temperatures were measured by replacing the sample with an NMR tube containing solvent and a copper–constantan thermocouple. The accuracy of the thermocouple was checked by measuring the temperature of a pentane slush obtained by adding liquid nitrogen to pentane.

(16) Nakanishi, H.; Fujita, H.; Yamamoto, O. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 214.

(17) Calculated spectra were generated by a VAX computer connected by a modem to an IBM PC equipped with a Radio Shack TRS-80 plotter–printer, and using a dynamic NMR program written by Binsch and Kleier: Binsch, G.; Klier, D. A. *QCPE* **1969**, *11*, 140.

(18) The difference in populations of the *E* isomers for vinyl formate and methyl formate should be larger in the same solvent, as indicated by the two entries for *tert*-butyl formate in Table I.

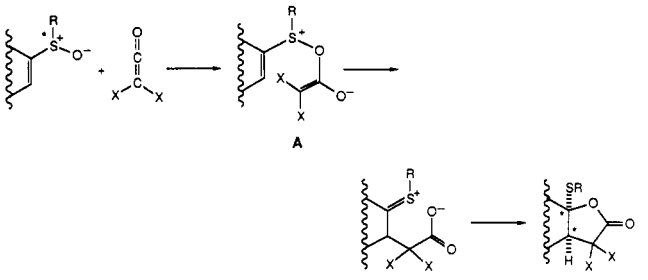
Reactions of Indole Sulfoxides with Dichloroketene: A New Approach to the Physostigmine Alkaloids

Summary: The reactions of 3-(phenylsulfinyl)- and 2-(methylsulfinyl)-*N*-(phenylsulfonyl)indoles with dichloroketene proceed at 0 °C to yield ring-fused butyrolactones **4** and **7**, respectively. Bicyclic indolines such as **7** can serve as intermediates in the synthesis of the physostigmine alkaloids.

Sir: Our recent reports[1] on the enantioselective lactonization of chiral vinyl sulfoxides with haloketenes have established this process as one of the most efficient protocols for chirality transfer from sulfur to carbon atoms. From a mechanistic standpoint this reaction proceeds via a 3,3-sigmatropic rearrangement of vinyloxysulfonium enolate system A as illustrated in Scheme I.

By analogy to other 3,3-sigmatropic rearrangements,[2] it was anticipated that the double bond of a vinyl sulfoxide could be part of a heteroaromatic ring. To this end, we investigated the reactions of indole derivatives having a

Scheme I



A

2- or 3-sulfinyl substituent.[3] At this time we report the successful lactonization of *N*-(arylsulfonyl)indole sulfoxides. Furthermore, the 2-substituted indoles serve as a unique precursors to be medicinally important physostigmine alkaloids **1**, which are anticholinesterases and miotics.[4] More recently, this alkaloid skeleton has been

(1) (a) Marino, J. P.; Perez, A. D. *J. Am. Chem. Soc.* **1984**, *106*, 7643. (b) Marino, J. P.; Fernandez de la Pradilla, R. *Tetrahedron Lett.* **1985**, *26*, 5382. (c) Marino, J. P.; Fernandez de Pradilla, R.; Laborde, E. *Synthesis* **1987**, 1088. (d) Marino, J. P.; Laborde, E.; Paley, R. *J. Am. Chem. Soc.* **1988**, *110*, 966.

(2) For a general review, see: Hill, R. K. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press, Inc.: New York, 1984; Chapter 8, p 503 in Vol. 3 (Part B).

(3) The analogous 2- and 3-(methylsulfinyl)benzofurans did not undergo the ketene–lactonization reaction at temperatures up to 110 °C. Only starting sulfoxides were recovered.

(4) For reviews, see: (a) Robinson, B. *The Alkaloids*; Manske, R. H. F., Ed.; Academic Press: New York, 1968; Vol. X, Chapter 5. (b) Robinson, B. *The Alkaloids*; Manske, R. H. F., Ed.; Academic Press: New York, 1971; Vol. XIII, Chapter 4.

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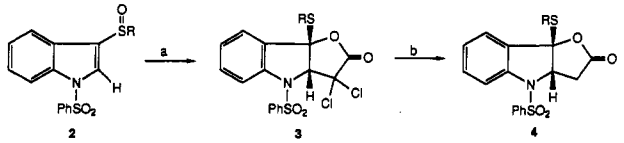
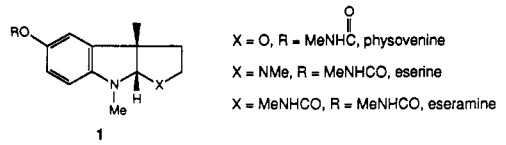
Scheme II[a]



[a] (a) 5 equiv of Cl_3CCOCl, 20 equiv of Zn(Cu), THF (0 °C); (b) 20 equiv of Al(Hg), THF–H_2O–MeOH (10:1:1).

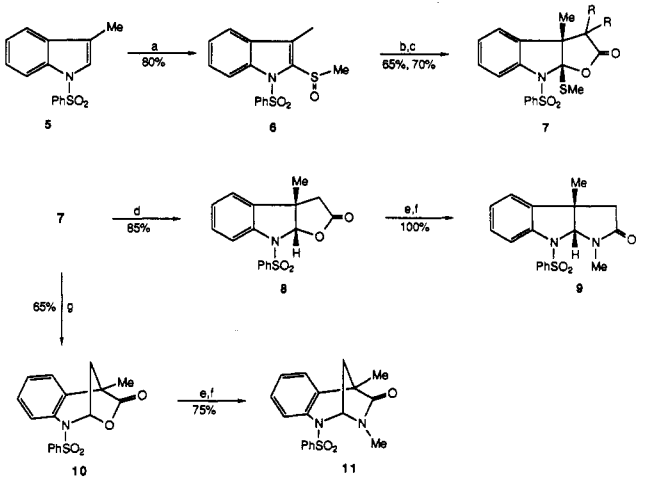
found to occur in the marine alkaloids from Broyoza Flustra foliacea in the flustramines.[5]



Our preliminary attempts at lactonizations of 3-sulfinylindoles quickly revealed that the basic nitrogen of indole must be protected in order to avoid reactions involving the nitrogen. Therefore, *N*-(phenylsulfonyl)-3-(phenylsulfinyl)indole (**2**, R = Ph) was prepared via a three-step procedure starting from indole. Deprotonation of indole with *n*-butyllithium at 0 °C followed by sulfenylation with phenyl disulfide yielded 3-(phenylthio)-indole.[7] Protection of the indole nitrogen was carried out by initial *n*-butyllithium deprotonation and quenching with benzenesulfonyl chloride; oxidation with *m*-chloroperbenzoic acid produced the protected indole 3-sulfoxide **2**. The reaction of **2** with dichloroketene as previously described[1] produced crystalline dichloro lactone[7] **3** in yields of 35–40%. Dechlorination of **3** with an excess of aluminum amalgam[8] led to the indoline-fused butyrolactone **4**. Thus, our initial premise that a heterocyclic aromatic system could participate in the 3,3-sigmatropic process of Scheme I was borne out (Scheme II).

Given the success of the 3-sulfinylindole system, our attention was focused on the analogous 2-sulfoxides since anticipated products of lactonization would serve as valuable precursors to the physostigmine skeleton **1**. Preparation of the requisite 2-sulfinylindoles **6** was accomplished by the direct sulfinylation of the 2-lithio-*N*-(phenylsulfonyl) derivative of skatetol[9] (see Scheme III). We suspected that the low yield of the lactone **3** derived from the 3-(phenylsulfinyl)indole **2** was due to the lower nucleophilicity of a diaryl-type sulfoxide system. When the 2-(phenylsulfinyl)indole analogous to **6** was reacted with dichloroketene, only a low yield (~10%) of the expected dichloro lactone could be realized. Employment of the methyl sulfoxide system **6** resulted in the formation of dichloro lactone **7** (R = Cl) in 65% yield. Chemoselective reduction to the dechlorinated lactone **7** (R = H) was effected with aluminum amalgam. To our knowledge, lactone **7** (R = H) is a unique bicyclic system containing a fully substituted carbon atom bearing three different

Scheme III[a]



[a] (a) 1.2 equiv of *n*-BuLi/THF (–23 °C), 5 equiv of MeSOCl; (b) 5 equiv of Cl_3CCOCl, 20 equiv of Zn(Cu), THF, 0 °C; (c) 20 equiv of Al(Hg), THF:H_2O:MeOH (10:1:1), room temperature; (d) 2 equiv of *n*-Bu_3SnH, cat. AIBN, PhH, 80 °C; (e) excess $MeNH_2$, 10 equiv 1 N HCl in anhy. MeOH (–78 °C); (f) cat. conc. H_2SO_4, DMF (115 °C, 1 h); (g) 2 equiv of DiBAL, CH_2Cl_2 (–78 °C).

heteroatoms.[10] This unusual functionalization of a carbon atom offers new possibilities for chemoselective transformations. For our purposes, the selective removal of the methylthio group would lead to the physostigmine system **1** (X = O, N).

The most successful desulfurization process was effected under free radical conditions of tri-*n*-butyltin hydride and AIBN, producing the indoline-fused lactone **8**. This lactone could be quantitatively converted to the corresponding indoline-fused lactam **9** with excess methylamine in acidic methanol followed by concentrated sulfuric acid to produce an obvious precursor to the eserine-type alkaloids **1**. The structure proof for lactone **8** and lactam **9** was complicated by results obtained from the reduction of thiomethyl lactone **7** with DiBAL at –78 °C. Under these conditions, lactone **10** was produced, which was isomeric with **8**, had an identical carbonyl stretch in the IR (1790 cm^{-1}) with **8**, but differed significantly in its ^1H NMR spectrum. Compound **8** possessed a methyl resonance at δ 1.67 (s) and a bridgehead hydrogen resonance at δ 6.8 (d) while compound **10** revealed corresponding resonances at δ 1.36 (s) and 6.21 (s), respectively. Further complexity was introduced when both lactones **8** and **10** were converted to lactams **9** and **11**, respectively.[10] These lactams were once again isomeric but differed significantly in their IR (**9**, CO at 1717 cm^{-1}; **10**, CO at 1701 cm^{-1}) and ^1H NMR spectra (**9**, CH_3, δ 1.53; **11**, CH_3, 0.67). Because of the

(5) Carle, J. S.; Christophersen, C. *J. Org. Chem.* **1980**, *45*, 1586.

(6) Recent syntheses of physostigmine and related compounds: (a) Wijnberg, J. B.; Speckamp, W. N. *Tetrahedron* **1978**, *34*, 2399. (b) Takano, S.; Goto, E.; Hirama, M.; Ogasawara, K. *Chem. Pharm. Bull.* **1982**, *30*, 2641. (c) Smith, R.; Livinghouse, T. *J. Org. Chem.* **1983**, *48*, 1554; *Tetrahedron* **1985**, *41*, 3559. (d) Shishido, K.; Kametani, T.; et al. *J. Org. Chem.* **1986**, *51*, 3007.

(7) All new compounds gave correct elemental analyses (±0.3) and possessed spectra (^1H NMR, ^{13}C NMR, MS, IR) consistent with the assigned structures. See footnote 10 for NMR data, and supplementary material for all spectral characterization.

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(9) Gribble, G. W., Saulnier, M. G.; Sibi, M. P.; Obaza-Nutaitis, J. A. *J. Org. Chem.* **1984**, *49*, 4518.

(10) Proton NMR spectra were recorded on a 300-MHz or 360-MHz Bruker instrument in $CDCl_3$. Compound **7a**: ^1H NMR 1.81 (3 H, s), 2.33 (3 H, s), 7.22 (1 H, t, J = 7.6), 7.32–7.38 (2 H, m), 7.47 (2 H, t, J = 7.6), 7.56 (1 H, t, J = 7.3), 7.69 (1 H, d, J = 8.0), 8.03 (2 H, d, J = 7.6). Compound **7b**: ^1H NMR 1.44 (3 H, s), 2.41 (3 H, s), 2.55 (1 H, d, J = 17.7), 2.72 (1 H, d, J = 17.7), 7.11–7.12 (2 H, m), 7.30 (1 H, m), 7.45 (2 H, t, J = 7.7), 7.55 (1 H, t, J = 7.4), 7.73 (1 H, d, J = 8.2), 7.99 (1 H, d, J = 8.0). Compound **8**: ^1H NMR 1.36 (3 H, s), 2.82 (1 H, d, J = 17.9), 2.95 (1 H, d, J = 17.9), 6.22 (1 H, s), 7.08–7.16 (2 H, m), 7.28 (1 H, td, J = 1.8, 8.0), 7.38 (1 H, d, J = 8.0), 7.50–7.63 (3 H, m), 8.03 (1 H, d, J = 7.7). Compound **9**: ^1H NMR 0.67 (3 H, s), 2.52 (1 H, d, J = 17.1), 2.70 (1 H, d, J = 17.1), 3.05 (3 H, s), 5.26 (1 H, s), 7.05 (1 H, d, J = 7.1), 7.16 (1 H, td, J = 0.9, 7.5), 7.32 (1 H, dt, J = 1.4, 7.8), 7.42 (2 H, t, J = 7.4), 7.56 (1 H, t, J = 7.4), 7.69–7.75 (3 H, m). Compound **10**: ^1H NMR 1.67 (3 H, s), 2.28 (1 H, d, J = 11.8), 2.61 (1 H, dd, J = 5.1, 11.8), 6.88 (1 H, d, J = 5.1), 7.05 (1 H, td, J = 0.8, 7.5), 7.18–7.21 (2 H, m), 7.42–7.52 (3 H, m), 7.78 (1 H, dd, J = 1.0, 8.7), 7.99 (2 H, d, J = 7.1). Compound **11**: ^1H NMR 1.53 (3 H, s), 1.68 (1 H, d, J = 11.2), 2.12 (1 H, dd, J = 4.3, 11.2), 2.93 (3 H, s), 6.00 (1 H, d, J = 4.3), 7.05 (1 H, t, J = 7.5), 7.20 (2 H, t, J = 8.0), 7.46–7.60 (3 H, m), 7.82 (3 H, d, J = 7.8).

presence of the *N*-(phenylsulfonyl) group, comparison of the chemical shifts and carbonyl stretches with analogous natural products was uninformative.

The structural assignments for **8**, **9**, **10**, and **11** were ultimately made after single-crystal analyses of lactone **10** and lactams **9** and **11** (see supplementary material for details).[11] The formation of the [3.2.1]bicyclic lactone **10** can be readily explained by the initial DiBAL reduction of the lactone carbonyl of **7** to the lactol followed by a ring opening to an aldehyde/thioester system, which undergoes a new ring closure of the sulfonamide anion onto the aldehyde carbonyl and expulsion of a thiomethyl group to form the amido acetal unit of **10**. This unusual series of events is just one manifestation of the unusual reactivity of the carbon atom bearing three different heteroatoms in **7**.

(11) Lactone **10** crystallized in the monoclinic space group $P2_1/c$, with a = 10.581 (2) Å, b = 9.157 (3) Å, c = 16.395 (5) Å, and β = 98.50 (2)°. The structure was solved with direct methods and refined to a R = 0.045 with a final R_w of 0.037. Lactam **9** crystallized in a nonstandard space group $I2/a$, with a = 18.716 (6) Å, b = 8.486 (4) Å, c = 21.237 (4) Å, and β = 98.26 (2)°. The structure was refined to a R = 0.040 with a final R_w = 0.037. Lactam **11** crystallized in the monoclinic space group $P2_1/c$, with a = 8.428 (3) Å, b = 8.586 (5) Å, c = 22.786 (13) Å, and β = 98.70 (4)°. The structure was solved with direct methods and refined to a R = 0.047 with a final R_w = 0.041.

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Supplementary Material Available: Summary of crystal data, fractional coordinates, thermal parameters, bond distances and angles, and perspective drawings for compounds **9**, **10**, and **11** and spectral characterization for compounds **7a**, **7b**, **8**, **9**, **10**, and **11** (27 pages). Ordering information is given on any current masthead page.

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A New Alkyllithium Reagent for the Direct Conversion of Aldehydes and Ketones to Vinylsilanes

Summary: [(Methoxydimethylsilyl)(trimethylsilyl)-methyl]lithium (**1**), which is readily formed in hydrocarbon solvent from silane **2** and *tert*-butyllithium, reacts with carbonyl compounds to yield the corresponding alkenylsilanes **3** via a Peterson-type reaction.

Sir: The vinylsilane group is a highly versatile synthon in organic synthesis.[1,2] In addition to serving as a latent carbonyl,[3] the trimethylsilyl group of alkenylsilanes can be replaced by a number of electrophiles to yield substituted alkenes. These reactions are generally of high yield and stereospecific.[2] Other net substitution reactions replace the trimethylsilyl group with alkyls, yielding either one of two possible isomers stereospecifically depending on the reaction conditions.[4] More recently 2,2-disubstituted alkenylsilanes have been shown to be precursors to alkylidene carbenes.[5]

Although there are a number of routes to vinylsilanes,[1,2,6,7] these have some important limitations. Since most of the reported syntheses utilize an alkyne,[2,8,9] only in rare cases have exocyclic alkenylsilanes been obtained.[10-12] [Bis(trimethylsilyl)methyl]lithium, the logical precursor to alkenylsilanes via the Peterson methodology,[13] is only effective with nonenolizable aldehydes and ketones.[14] We now report on a new lithium reagent, [(methoxydimethylsilyl)(trimethylsilyl)methyl]lithium (**1**),

Scheme I

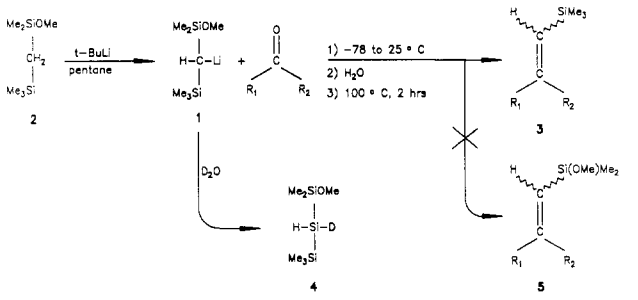

Table I. Yields and Isomer Ratios of Alkenylsilanes $R_1(R_2)C{=}C(H)SiMe_3$

carbonyl compound	product	R_1	R_2	yield, %[a]	*E*:*Z*
cyclohexanone	**3a**	$-(CH_2)_5-$		68[b]	
2-cyclohexen-1-one	**3b**	$-CH{=}CH(CH_2)_3-$		61[c]	2:1
3-pentanone	**3c**	Et	Et	70[c]	
benzaldehyde	**3d**	Ph	H	85[d,e]	3:1

[a] Isolated yields. [b] See ref 10 and 11. [c] Spectral and analytical data available in supplementary material. [d] Quantitative by NMR. [e] See ref 21.

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