(1 H, dt, J = 7.5, 1.2 Hz, H-10), 6.81 (1 H, br d, J = 7.5, H-12), 3.62 (3 H, s, CO_2CH_3), 3.21 (1 H, br dt, J = 12.0, 2.3 Hz, H-3α), 3.19 (3 H, s, NCH_3), 2.65 (1 H, s, H-21), 2.04 (1 H, ddd, J = 12.0, 11.0, 3.5 Hz, H-3β), 1.57 (1 H, m, H-14α), 1.40 (2 H, m, H-14β, H-15α), 0.91 (1 H, br dt, J = 12.5 3.5, 1.0 Hz, H-15β); ^{13}C NMR (50.4 MHz, $CDCl_3$; the chemical shift values in parentheses are those reported in ref 3a) 179.3 (179.4, C-2), 53.8 (53.8, C-3), 55.1 (55.2, C-5), 36.5 (36.5, C-6), 55.2 (55.1, C-7), 133.7 (134.0, C-8), 126.8 (126.9, C-9), 121.7 (121.8, C-10), 127.3 (127.5, C-11), 107.7 (107.8, C-12), 142.3 (142.4, C-13), 21.4 (21.4, C-14), 31.2 (31.2, C-15), 28.0 (28.0, C-16), 30.9 (30.9, C-17), 7.8 (7.9, C-18), 26.3 (26.3, C-19), 39.2 (39.3, C-20), 76.6 (76.7, C-21), 174.3 (174.4, CO_2CH_3), 51.3 (51.2, OCH_3), 26.3 (26.3, NCH_3); CD (MeOH) $\Delta\epsilon$ +2.23 (287 nm), +5.54 (260), 0 (249), −10.42 (231) [lit.[3a] (THF) $\Delta\epsilon$ −3.22 (287 nm), −8.51 (260), 0 (250), +13.6 (238). Anal. Calcd for $C_{22}H_{30}N_2O_3$: C, 71.32; H, 8.16; N, 7.56. Found: C, 71.26; H, 8.19; N, 7.50.

Equilibration of 12 in Chloroform. A 2-mL sample of a 2 × 10^{-2} M solution of **12** in $CDCl_3$ was kept at 35 °C. At 0.5, 1.6, 4.0, and 6.0 h, a ^{1}H NMR spectrum of the sample was recorded and the optical rotation measured. Ratios of **12/13/14/15** calculated from the areas of methoxy peaks and $[\alpha]^{20}_D$ at the appropriate time are reported: 0.5 h (92:5:3:1), −7.4°; 1.6 h (83:10:5:1), −10.2°; 4.0 h (72:20:7:1), −11.9°; 6.0 h (71:21:7:1), −12.4°. No change in optical rotation of the solution was observed after this time.

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Registry No. **2a**, 3247-10-7; **3**, 88377-49-5; **6**, 88377-50-8; **7**, 88377-51-9; **8**, 88424-28-6; **9**, 79854-75-4; **10**, 88377-52-0; **11**, 88377-53-1; **12**, 23185-53-7; **13**, 88424-29-7; **14**, 88424-30-0; **15**, 88424-31-1; trimethyl phosphonoacetate, 5927-18-4.

Regioselective Functionalization of Heterocyclic Rings: Synthesis and Reactions of 1-Methyl-2-(trimethylsiloxy)pyrrole and 2-(Trimethylsiloxy)thiophene

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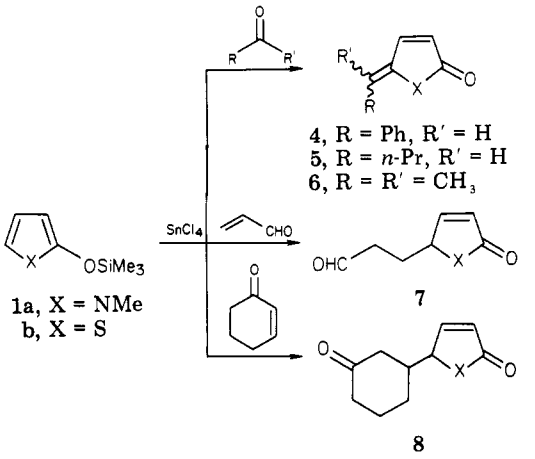
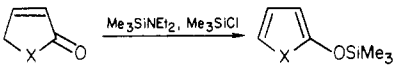
Recently we reported a novel synthesis of 2-(trimethylsiloxy)furan and its regiospecific functionalization with representative nucleophilic and electrophilic reagents.[1] We now report the synthesis of the previously unknown 1-methyl-2-(trimethylsiloxy)pyrrole (**1a**) and 2-(trimethylsiloxy)thiophene (**1b**) and their use as synthetic units for the preparation of regioselectively substituted unsaturated lactams and thiolactones.

Our approach involved interaction of amino and thiosilanes with 1-methylpyrrol-2(5*H*)-one (**2a**) and thiophen-2(5*H*)-one (**2b**). Thus, addition of (diethylamino)trimethylsilane (Me_3SiDEA) to an equimolar amount of

Scheme I



pyrrolone **2a**, under mild conditions, gave **1a** in 70% yield (eq 1). From **2b**, following the same procedure, **1b** was



(1)

2a, X = NMe
b, X = S

1

detected in the reaction mixture at −78 °C but rapidly decomposed at room temperature, probably owing to the presence of diethylamine produced during the reaction. Addition of 2 equiv of trimethylchlorosilane (Me_3SiCl) and 1.2 equiv of Me_3SiDEA to **2b** gave **1b** in 65% yield, after distillation, as a colorless oil that could be kept indefinitely under an inert atmosphere.

In contrast with the behavior of 2(5*H*)-furanone with the same reagents, no products of nucleophilic substitution at position 4 were isolated in these reactions with **2a** and **2b**. The action of $PhSSiMe_3$ on **2a** and **2b** again resulted in the formation of **1a** and **1b**, but sizable amounts of the 4-substituted products **3a** and **3b** were also recovered from the reaction mixture[2] (eq 2); with $Me_3SiSSiMe_3$ and

(2)

3a, X = NMe
b, X = S

2

1

Me_3SiSMe, on the other hand, siloxy compounds **1a** and **1b** were predominant, and only trace amounts of the corresponding 4-substituted products were detected by ^{1}H NMR analysis.

Both **1a** and **1b** behave as heterocyclic analogues of siloxy dienes; in the presence of $SnCl_4$ or $AlCl_3$[3] as Lewis acid catalysts, they reacted with various carbon electrophiles to give, after a hydrolytic workup, methylenepyrrolones or -thiophenones **4a,b** with benzaldehyde, **5a,b** with butyraldehyde, and **6a,b** with acetone (Scheme I). Compounds **4a** and **5a** were mixtures of *Z* and *E* isomers in an approximate 1:1 ratio as revealed by ^{1}H NMR spectra: in fact, the signals of the unsaturated and heteroaromatic protons showed a multiplicity which was unaffected by spin decoupling experiments, suggesting the presence of two geometrical isomers. No attempts were

(1) Fiorenza, M.; Ricci, A.; Romanelli, N.; Taddei, M.; Dembech, P.; Seconi, G. *Heterocycles* **1982**, *19*, 2327.

(2) On carrying out the reaction with PhSH and **2a** or **2b**, without solvent, **3b** was obtained after 6 h at 100 °C in 75% yield, but **3a** was identified in a complex reaction mixture arising after warming at 100 °C for 2 h.

(3) Attempts to use a fluoride ion catalyst led to complex products and were abandoned.

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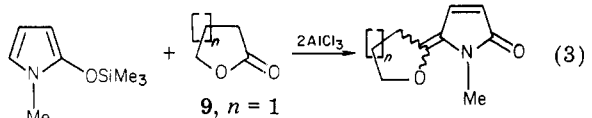
Table I. Products of Regioselective Functionalization of 1a and 1b with Carbon Electrophiles

compd[a]	Lewis acid (mmol)	reaction time, h (temp, °C)	chromatog eluent[b]	% yield	MS (M^+), m/e	^1H NMR ($CDCl_3/Me_4Si$), δ
4a[c]	$SnCl_4$ (3)	1 (−78), 6 (25)	MeCN/EtAc (10/1)	45	185	3.21 (s, 3 H, NCH_3), 6.29 (d, 1 H, J = 6 Hz, CH-CO), 6.30 (d, 1 H, J = 6.5 Hz, CH-CO), 6.45 (d, 1 H, J = 6 Hz, Ph-CH), 6.47 (d, 1 H, J = 6.5 Hz, Ph-CH), 7.4 (m, 6 H, aromatic and =C—CH)
4b[d]	$SnCl_4$ (3)	1 (−78), 48 (25)	*n*-Hex/EtAc (15/1)	57	188	6.34 (d, 1 H, J = 6 Hz, CH-CO), 7.03 (s, 1 H, Ph-CH), 7.4 (m, 5 H, aromatic), 7.66 (d, 1 H, J = 6, Hz, =C—CH)
5a[c]	$SnCl_4$ (3)	1 (−20), 6 (25)	*n*-Hex/EtAc (1/5)	84	151	0.9 (m, 3 H, CH_3), 1.5 (m, 2 H, CH_2), 2.3 (m, 2 H, CH_2—C=), 3.10 (s, 3 H, NCH_3), 5.4 (m, 1 H, CH=C), 6.18 (d, 1 H, J = 6 Hz, =C—CO), 6.19 (d, 1 H, J = 6 Hz, =C—CO), 7.22 (d, 1 H, J = 6 Hz, =CCH=), 7.24 (d, 1 H, J = 6 Hz, =C—CH)
5b[d]	$SnCl_4$ (3)	1 (−20), 1 (25)	MeOH	46	154	1.0 (m, 3 H, CH_3), 1.5 (m, 2 H, CH_2), 2.3 (m, 2 H, CH_2—C 6.3 (br, 2 H, CH=C and CH—CO), 7.51 (d, 1 H, J = 6 Hz, =C—CH)
6a	$SnCl_4$ (3)	6 (−78)	*n*-Hex/EtAc (5/1)	68	137	1.95 (s, 3 H, CH_3), 2.10 (s, 3 H, CH_3), 3.23 (s, 3 H, NCH_3), 5.90 (d, 1 H, J = 6 Hz, CH—CO), 7.12 (d, 1 H, J = 6 Hz, =C—CH)
6b	$SnCl_4$ (3)	1 (−78), 16 (25)	*n*-Hex/EtAc (1/1)	60	140	2.05 (s, 3 H, CH_3), 2.15 (s, 3 H, CH_3), 6.30 (d, 1 H, J = 6 Hz, CH—CO), 7.85 (d, 1 H, J = 6 Hz, =C—CH)
7a	$SnCl_4$ (0.15)	2 (−78)	MeOH	48	153	1.9-2.5 (br, 4 H, CH_2-CH_2), 2.98 (s, 3 H, NCH_3), 4.1 (m, 1 H, CH—N), 6.2 (m, 1 H, =CH—CO), 7.0 (m, 1 H, =C—CH), 9.8 (m, 1 H, CHO)
7b	$SnCl_4$ (0.15)	4 (−78)	*n*-Hex/EtAc (1/1)	38	156	1.8-2.3 (br, 4 H, CH_2-CH_2), 4.4 (m, 1 H, CH-S), 6.1 (m, 1 H, =CH—CO), 7.3 (m, 1 H, =C—CH), 9.6 (m, 1 H, CHO)
8a	$SnCl_4$ (3)	1 (−78)	*n*-Hex/EtAc (1/2)	38	193	1.5-2.5 (br, 9 H, cycloexanone), 2.86 (s, 3 H, NCH_3) 4.2 (m, 1 H, CH-N), 6.2 (m, 1 H, =CH—CO), 7.1 (m, 1 H, =C—CH)
8b	$SnCl_4$ (3)	2 (−78)	*n*-Hex/EtAc (1/5)	83	196	1.5-2.7 (br, 9 H, cyclohexanone), 4.6 (m, 1 H, CH-S), 6.3 (m, 1 H, =CH—CO), 7.5 (m, 1 H, =C—CH)
11	$AlCl_3$ (7)	1 (−78), 24 (25)	Me_2CO/*n*-Hex (5/1)	41	165	1.9-2.3 (br, 4 H, $(CH_2)_2$), 3.37 (s, 3 H, NCH_3), 4.4 (m, 2 H, CH_2-O), 5.94 (d, 1 H, J = 5 Hz, =CH—CO), 7.01 (d, 1 H, J = 5 Hz, =C—CH)
12	$AlCl_3$ (7)	1 (−78), 24 (25)	Me_2CO/*n*-Hex (2/1)	68	193	1.6-1.9 (br, 6 H, $(CH_2)_3$), 2.4 (m, 2 H, CH_2—C=) 3.30 (s, 3 H, NCH_3), 4.1 (m, 2 H, CH_2-O), 6.31 (d, 1 H, J = 6 Hz, CH—C=O), 7.06 (d, 1 H, J = 6 Hz, =C—CH)

[a] Elemental analyses (C, H, N) for all compounds were within ±0.3% of the calculated values. [b] Separation for all compounds was carried out by PTLC except for 11 and 12 (purified by Chromatospac and column chromatography, respectively). [c] Mixture of *Z* and *E* isomers in 1:1 ratio on ^1H NMR analysis. [d] Only one geometrical isomer was detectable at ^1H NMR analysis.

made to separate these compounds by TLC. With acrolein and 2-cyclohexenone, the 1,4-addition products **7a,b** and **8a,b** were obtained in good to high yields (38–83%). In all cases the substitution reactions were regiospecific in that only C-5 was attacked, no reaction being seen at C-3.

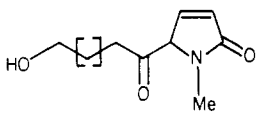
Whereas $SnCl_4$ proved to be the most effective Lewis acid catalyst in the functionalization of **1a** and **1b** with all the carbonyl electrophiles, the corresponding reaction with saturated lactones was successful only with **1a** in the presence of 2 equiv of $AlCl_3$. Moreover only γ-butyrolactone (**9**) and ε-caprolactone (**10**) were found to react to give, after a hydrolytic workup, compounds **11** and **12** (eq 3).



(3)

1a **9**, $n = 1$; **10**, $n = 3$ **11**, $n = 1$; **12**, $n = 3$

Most likely compounds **11** and **12** were generated through compound **13** which undergoes intramolecular cyclization under the acidic workup conditions.



13

The regiospecific electrophilic substitution at position 5 of 2(5*H*)-pyrrolone and 2(5*H*)-thiophenone ring systems starting from the corresponding siloxy heterocycles appears synthetically attractive, being somewhat simpler than the methods previously reported in the literature for compounds listed in Table I[4-6] and much more general in that it can be extended to a much wider range of electrophiles.

The general scope and the limits of this reaction are currently being considered.

Experimental Section

Boiling points were uncorrected. ^1H NMR spectra were obtained on a Perkin-Elmer R-32 90-MHz spectrometer; chemical shifts are reported in δ units downfield from internal Me_4Si. IR spectra were recordered in CCl_4 or as a liquid film with NaCl cells on a Perkin-Elmer 283 spectrophotometer; mass spectra and GC/MS were determined on a Varian Matt 111 instrument equipped with an OV-101 5% column. Preparative TLC were carried out on E. Merck silica gel F plates and visualized by ultraviolet lights; column chromatography was carried out with a 25-cm column filled with silica gel containing $CaSO_4$ or with a Jobin Yvon Chromatospac preparative column with silica gel (H-60, 15 μm). Microanalysis was performed with a Perkin-Elmer 240 C analyzer. Compounds **1a** and **1b** were prepared according to Baker[7] and Hawkins,[8] respectively; the silylating reagents are commercially available from Aldrich Chemical Co. and Fluka AG chemicals.

1-Methyl-2-(trimethylsiloxy)pyrrole (1a). To a cooled solution (0 °C) of 1.45 g (10 mmol) of Me_3SiDEA in dry Et_2O (2 mL) under nitrogen atmosphere and with magnetic stirring was added a solution of 0.97 g (10 mmol) of **2a** dropwise. The reaction mixture was allowed to warm to room temperature, and the conversion was judged, by ^1H NMR and GC analyses, to be complete after 12 h. Evaporation of the crude reaction mixture followed by vacuum distillation afforded **1a**: 1.18 g (70% yield); bp 64–65 °C (7.5 mmHg); IR (CCl_4) 3100, 2960, 1250, 920, 870, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.35 (s, 9 H, Si $(CH_3)_3$), 3.41 (s, 3 H, NCH_3), 5.25 (m, 1 H, heterocyclic ring), 5.93 (m, 1 H, heterocyclic ring), 6.17 (m, 1 H, heterocyclic ring). Anal. Calcd for $C_8H_{15}NOSi$: C, 56.80; H, 8.87; N, 8.28. Found: C, 56.62; H, 8.89; N, 8.27.

2-(Trimethylsiloxy)thiophene (1b). To a cooled solution (−78 °C) of 5.00 g (50 mmol) of **2b** and 10.8 g (100 mmol) of Me_3SiCl in dry Et_2O (25 mL) under nitrogen atmosphere and with mechanical stirring was added a solution of 7.25 g (50 mmol) of Me_3SiDEA in 25 mL of dry Et_2O dropwise. After 4 h at −78 °C, GC analysis of the reaction mixture again revealed the presence of **2b** that was completely converted into **1b** by addition of 1.08 g (7 mmol) of Me_3SiDEA. Et_2NH–HCl was filtered off and the solvent evaporated to give, after vacuum distillation, **1b**: 5.59 g (65% yield); bp 50–52 °C (0.75 mmHg); IR (CCl_4) 3080, 2960, 1570, 1250, 870, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.38 (s, 9 H, $Si(CH_3)_3$), 6.15 (m, 1 H, heterocyclic ring), 6.55 (m, 1 H, heterocyclic ring), 6.70 (m, 1 H, heterocyclic ring). Anal. Calcd for $C_7H_{12}OSSi$: C, 48.82; H, 6.98. Found: C, 48.68; H, 6.99.

General Procedure for the Preparation of 3a and 3b. An equimolar mixture of $PhSSiMe_3$ and **2a,b** was maintained at room temperature under nitrogen and with magnetic stirring for 10 h. Compounds **1a** and **1b** were removed under vacuum, affording crude **3a,b** which were further purified by fractional distillation.

3a: bp 75 °C (0.03 mmHg); 60% yield; IR (liquid film) ν_{CO} 1695 cm^{-1}; ^1H NMR (CCl_4) δ 2.75 (s, 3 H, NCH_3), 3.2–3.4 (m, 2 H, CO–CH_2), 3.7–3.9 (m, 2 H, N–CH_2), 3.9–4.2 (m, 1 H, CH–S), 7.40 (m, aromatics); MS, *m/e* 207 (M^+, base). Anal. Calcd for $C_{11}H_{13}NOS$: C, 63.77; H, 6.27; N, 6.75. Found: C, 63.96; H, 6.26; N, 6.73.

3b: bp 113–115 °C (0.11 mmHg); 45% yield; IR (liquid film) ν_{CO} 1705 cm^{-1}. ^1H NMR δ 2.3–3.0 (m, 2 H, CO–CH_2), 3.2–3.7 (m, 2 H, S–CH_2), 3.7–4.1 (m, 1 H, S–CH), 7.45 (m, 5 H, aromatics); MS, *m/e* 210 (M^+, base). Anal. Calcd for $C_{10}H_{10}OS_2$: C, 57.13; H, 4.75. Found: C, 57.29; H, 4.74.

General Procedure for the Regioselective Functionalization of the Heterocyclic Rings 1a and 1b with Electrophiles. To a cooled (−78 °C) solution of 3 mmol of **1a** or **1b** and of the appropriate electrophile (3 mmol) in dry CH_2Cl_2 (5 mL) under an argon atmosphere and with magnetic stirring was rapidly added the required amount of Lewis acid catalyst (see Table I). The hydrolytic workup with HCl 0.1 N solution followed by evaporation of the organic layer afforded crude substituted unsaturated lactams and thiolactones **4–12**, which were obtained as colorless or yellow oils after purification by PTLC or column chromatography on silica gel (see Table I). Only compounds **4a** and **4b** slowly solidified on standing to waxy materials.

Registry No. **1a**, 87884-52-4; **1b**, 83043-44-1; **2a**, 13950-21-5; **2b**, 3354-32-3; **3a**, 87884-53-5; **3b**, 87884-54-6; (*E*)-**4a**, 87884-55-7; (*Z*)-**4a**, 87884-56-8; **4b**, 13755-25-4; (*E*)-**5a**, 87884-57-9; (*Z*)-**5a**, 87884-58-0; **5b**, 6542-68-3; **6a**, 78210-72-7; **6b**, 87884-59-1; **7a**, 87884-60-4; **7b**, 87884-61-5; **8a**, 87884-62-6; **8b**, 87884-63-7; **9**, 96-48-0; **10**, 502-44-3; **11**, 87884-64-8; **12**, 87884-65-9; Me_3SiDEA, 996-50-9; Me_3SiCl, 75-77-4; $PhSSiMe_3$, 4551-15-9; $Me_3SiSSiMe_3$, 3385-94-2; Me_3SiSMe, 3908-55-2; $SnCl_4$, 7646-78-8; $AlCl_3$, 7446-70-0; benzaldehyde, 100-52-7; butyraldehyde, 123-72-8; acetone, 67-64-1; acrolein, 107-02-8; 2-cyclohexenenone, 930-68-7.

(4) Jakobsen, H. J.; Larsen, E. H.; Lawesson, S. O. *Tetrahedron* **1964**, *19*, 1867.
(5) Bocchi, V.; Gardini, G. P. *Tetrahedron Lett.* **1971**, 211.
(6) Plieninger, H.; Bauer, H.; Katritzky, A. R.; Lerch, U. *Justus Liebigs Ann. Chem.* **1962**, *654*, 165.
(7) Baker, J. T.; Sifniades, S. *J. Org. Chem.* **1979**, *44*, 2798.
(8) Hawkins, R. T. *J. Heterocycl. Chem.* **1974**, 291.

A Short Synthesis of 4,5-Methanochrysene and 6-Oxo-7-oxabenzo[*a*]pyrene,[1] Two Benzo[*a*]pyrene Analogues

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Methylated polynuclear aromatic hydrocarbons are often more carcinogenic than the parent derivatives. It is known that the bay region methylated 5-methylchrysene (**1**) is a

(1) Conventional numbering system used for benzo[*a*]pyrene derivatives. See structure **5**.

0022-3263/84/1949-0553$01.50/0