SYNTHESIS AND CHARACTERIZATION OF 3,4-DI-1-BUTYLFURAN, PYRROLE, AND SELENOPHENE

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Abstract: 3,4-Di-t-butylfuran (1), pyrrole (2), and selenophene (4) were first synthesized using 3,4-di-t-butylthiophene (3) as the starting material and these overcrowded five-membered hetarenes including 3 were characterized by NMR and MMP2 calculations.

Five-membered heteroaromatic compounds carrying two *t*-butyl groups on adjacent positions are overcrowded and strained because of nonbonded repulsion between bulky *t*-butyls. Calculations have shown that strain energies increase in the order of 3,4-di-*t*-butylfuran (1), pyrrole (2), and thiophene (3) and are very large.¹ Among them, however, only 3 has been successfully synthesized.²⁻⁶ We have recently developed a simple synthesis of 3 and its oxidative conversion into 3,4-di-*t*-butylthiophene 1,1-dioxide (5) in high yield, which enables the preparation of these compounds in large quantities.³ We report here the first synthesis of 1, 2, and 3,4-di-*t*-butyl-selenophene (4)⁷ using 3 or 5 as the starting material. Also reported is the characterization of these compounds including 3 by NMR and MMP2 calculations.

Flash vacuum pyrolysis of thiophene 1,1-dioxides, in some cases, affords the corresponding furans as one of the major products.⁸ Application of this methodology to the dioxide 5 furnished 3,4-di-*t*-butylfuran (1) as a colorless liquid (bp 40 °C/17 mmHg, bulb-to-bulb distillation) in 12% yield, when **5** was pyrolyzed at 400 °C/0.2 mmHg.

Reaction of thiophene with ethoxycarbonylnitrene, generated by thermal decomposition of ethyl azidoformate, produces a low yield of *N*-ethoxycarbonylpyrrole.⁹ We then examined the reaction of the thiophene **3** with tosylnitrene,¹⁰ generated by thermal decomposition of tosyl azide, with the expectation of obtaining *N*-tosyl-3,4-di-*t*-butylpyrrole (6). Thus, heating a mixture of **3** (10 mmol) and tosyl azide (3.3 mmol) at 150 °C for 5 h under nitrogen afforded a complex mixture, from which the expected 6^{11} was isolated in a yield less than 10% by repeated purification by column chromatography. Alkaline hydrolysis of **6** produced **2** in 93% yield as colorless crystals, mp 133-134 °C.

4473

Our previous failure¹² in the synthesis of the selenophene 4 via intramolecular dicarbonyl coupling, the method used for the preparation of 3, forced us to devise a new strategy. The new approach involves the reaction of the dioxide 5 with elemental selenium. Fortunately, the reaction worked to give 4 as a crystalline compound, mp 51-52 °C, in 21% yield, when 5 was heated with selenium powder at 210 °C for 8 h using benzene as the solvent in a stainless steel autoclave. A small amount of reduced 3 was formed as a byproduct. The selenophene synthesis developed here seems to have some generality. Thus, heating 3,4-diphenylthiophene 1,1-dioxide and selenium in refluxing o-dichlorobenzene afforded 3,4-diphenylselenophene in 23% yield.



¹H and ¹³C NMR data of compounds 1-4 (CDCl₃ as the solvent) are summarized in Table 1. Both of the *t*-butyls and the ring protons are equivalent in every compound and appear as singlets, except for **2**, where the ring protons appear as a doublet with J=2.7 Hz because of the coupling with the hydrogen on nitrogen. For comparison ¹H NMR chemical shift values at the 2-position of the parent compounds and 3,4-dimethyl derivatives are listed in Table 2.¹³ In every case the chemical shift values of **1-4** lies between those of the corresponding parent compounds and of dimethyl derivatives. The Table also includes the difference (δ H- δ Me) of the chemical shift values between parent compounds and the corresponding dimethyl derivatives and the difference (δ H- δ He) of the chemical shift values between parent compounds and the corresponding dimethyl derivatives. The electron-releasing ability of methyl and *t*-butyl is much the same¹⁴ and thus the upfield shift caused by an electronic effect is expected to be similar for these two substituents. Therefore the difference [(δ H- δ Me)-(δ H- δ t-Bu)](= δ t-Bu- δ Me), which increases in the order of furan, pyrrole, selenophene, and thiophene, should reflect the degree of steric strain in each system.

Table 3 shows the % change of the bond lengths and bond angles, obtained by MMP2 calculations,¹⁵ on going from the parent compounds to the di-*t*-butyl compounds **1-3**.¹⁶ The largest change of the bond lengths generally occurs at the C₃-C₄ bond and that of the bond angles at the *t*-butyl-C₃-C₄ angle, indicating that nonbonded repulsion between *t*-butyls is mainly attenuated by enlarging the bond length C₃-C₄ and the bond angle *t*-Bu-C₃-C₄. This tendency increases in the order of furan, pyrrole, and thiophene, which is reflected in the magnitude of the strain energies. Thus, the increase of the steric energy on going from the parent compounds to di-*t*-butyl compounds is calcualted to be 14.0 kcal/mol for furan, 15.7 kcal/mole for pyrrole, and 20.8 kcal/mole for thiophene. Finally It should be stressed that steric energies obtained here well correlate with the deviation of the chemical shift values ($\delta_{Me}-\delta_t$ -Bu).

Compounds	¹ H NMR					
	ring proton	t-Bu	C ₂ (C ₅)	C3(C4)	C <u>Me</u> 3	<u>C</u> Me ₃
1	7.20	1.36	140.3	133.9	32.5	31.1
2	6.66	1.40	116.5	131.5	33.3	31.7
3	7.16	1.47	122.3	150.6	33.5	35.3
4	7.80	1.48	126.3	152.6	33.7	36.9

Table 1 NMR Chemical Shift Values (δ) of Compounds 1-4

Table 2 Chemical Shift of C₂-H of the Parent Compounds and 3,4-Dimethyl Derivatives and Difference of Effect of Methyl and t-Butyl on Upfield Shift

	Parent Compounds	Dimethyl Derivatives	δ _H -δ _{Me}	δ _Η -δ _{t-Bu}	(δ _H -δ _{Me})-(δ _H -δ _{f-Bu})
Furan	7.29	7.11	0.18	0.09	0.09
Pyrrole	6.68	6.49	0.19	0.02	0.17
Thiophene	7.18	6.79	0.39	0.02	0.37
Selenophene	7.88	7.47	0.41	0.08	0.33

Table 3 Relevant % Change of Bond Lengths and Bond Angles on Going from Parent Compounds to the Corresponding Di-t-butyl Derivatives

R R	% change = $\frac{(t-Bu-H)}{H} \times 100$					
~ (- <u>x</u>	L12	L ₂₃	L34	A437	A326
н∽бх∕≥н	0	-1.65	0.54	1.17	5.58	4.40
1 0	NH	-0.90	0.59	1.31	5.89	4.74
L: Bond Length A: Bond Angle	S	-0.40	0.62	1.99	6.76	4.77

References and Notes

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No report has appeared on the successful synthesis of selenophenes having t-butyls on adjacent positions.

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11. Mp 106-107 °C; ¹H NMR (CDCl₃) δ 1.32 (s, 18H, t-Bu), 2.41 (s, 3H, Me), 6.94 (s, 2H, pyrrole ring),

7.29 (d, 2H, benzene ring), 7.70 (d, 2H, benzene ring); ¹³C NMR (CDCl₃) δ 21.6 (q), 32.3 (s), 32.6 (q), 118.5 (d), 126.7 (d), 129.8 (d), 136.4 (s), 137.8 (s), 144.4 (s).

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16. Calculated bond lengths (angstrom): 1; L₁₂ 1.342, L₂₃ 1.371, L₃₄ 1.444: 2; L₁₂ 1.359, L₂₃ 1.390, L₃₄
1.429: 3; L₁₂ 1.704, L₂₃ 1.377, L₃₄ 1.451. Calculated bond angles (°): 1; A₃₂₆ 131.1, A₄₃₇ 134.2: 2; A₃₂₆
131.2, A₄₃₇ 133.8: 3; A₃₂₆ 126.7, A₄₃₇ 132.2. MMP2 calculations were not attained on selenophenes.