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SYNTHESIS OF 1,4-DIHYDROPYRROLO[3,2-b] PYRROLE[1]

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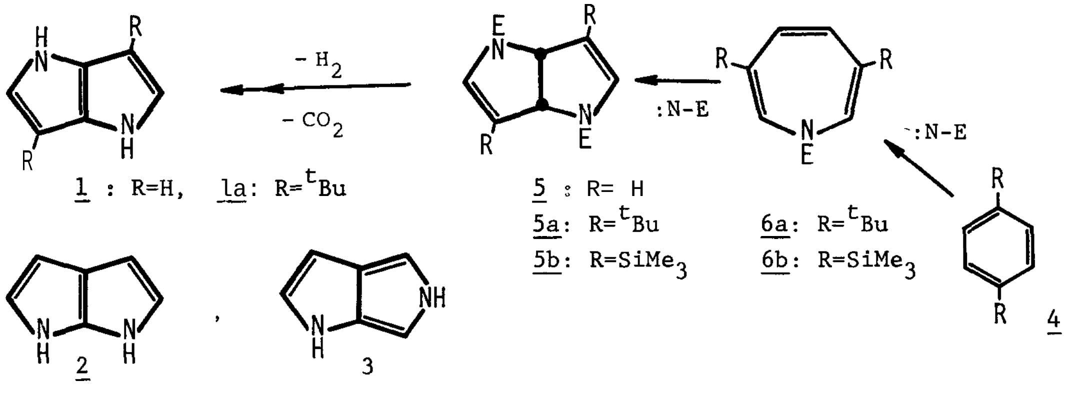
Summary: Dihydropyrrolo[3,2-b]pyrrole 1 was synthesized starting from 1,4-bis(trimethylsilyl)benzene.

Dihydro derivatives of diazapentalenes, which are named as dihydropyrrolo-[3,2-b]-, pyrrolo[2,3-b]-, and pyrrolo[3,4-b]pyrrole, 1-3, are classified as novel 10π-aromatic compounds. They are isoelectronic with pentalenyl dianion or indole. Although thienothiophenes and thienopyrroles have been investigated in some details,[2] the chemistry of pyrrolopyrroles has not been explored because of the synthetic barrier.[3] In previous papers, we described the preparation of the 3,6-di-tert-butyl derivative (1a) of pyrrolo[3,2-b]-pyrrole.[6,7] In order to clarify the chemical properties of this system, we have developed a synthetic approach for the parent compound 1.



1 : R=H, 1a: R=^{t}Bu

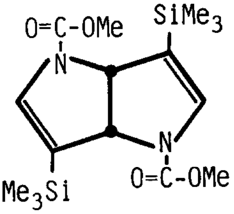
5 : R= H
5a: R=^{t}Bu
5b: R=$SiMe_3$

6a: R=^{t}Bu
6b: R=$SiMe_3$

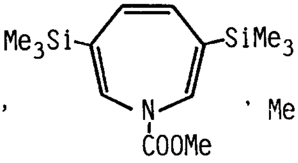
4

2 3

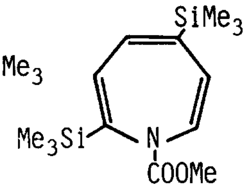
Compound 1a had been synthesized using nitrene addition reaction with p-di-tert-butylbenzene (4a),[6] where the existence of two tert-butyl groups in the para-position was necessary for the formation of the one-to-two adduct 5a. It was unsuccessful to obtain the similar one-to-two adduct 5 with benzene itself. However, it might be expected that the substitution of bulky trimethylsilyl group on benzene ring is effective for two step addition of nitrene via azepine intermediate 6b to give bicyclic framework 5b, which will be a potential precursor of pyrrolo[3,2-b]pyrrole.



5b ,



6b ,



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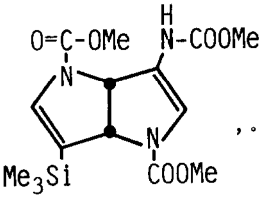
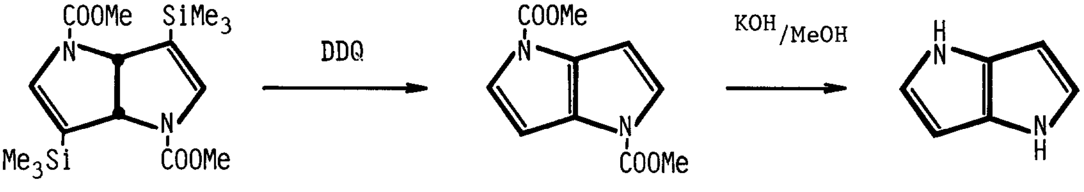


8b , . . .

When a half molar equivalent of methyl azidoformate was added to an efficiently stirred flask containing 1,4-bis(trimethylsilyl)benzene (4b) at 130°C, an expected one-to-two adduct, N,N-dimethoxycarbonyl-4,8-bis(trimethylsilyl)-2,6-diazabicyclo[3.3.0]octa-3,7-diene (tetrahydropyrrolo[3,2-b]pyrrole 5b[8]), mp 118-119°C, was obtained in 9% yield along with two kinds of azepines, 6b[9] and 7b[9]. The NMR spectrum of the bicyclic adduct 5b suggests the symmetric structure but the spectral patterns are somewhat complicated at 30°C. At elevated temperatures, simplification of spectrum could be observed : ^{1}H-NMR (90MHz, in CDCl$_3$) δ 0.13 (18H, s), 3.77 (6H, s), 5.43 (2H, s), 6.65 (2H, s) ; ^{13}C-NMR (22.6MHz, in CDCl$_3$) δ 0.0 (q, SiMe), 53.7 (q, OMe), 70.3 (d, C$_1$ and C$_5$), 119.8 (s, C$_4$ and C$_8$), 139.4 (d, C$_3$ and C$_7$), 153.3 (s, CO) at 60°C. This temperature dependency of the NMR spectra is probably attributed to conformational change of the N-carbomethoxy moieties influenced by the bulky trimethylsilyl group. The activation energy, which was estimated to be 16 kcal/mol by dynamic NMR method, is reasonable for the C-N bond rotation of urethane moiety.[10] Under similar reaction condition 3,6-bis(trimethylsilyl)-1H-azepine 6b afforded the rearranged nitrene adduct 5b in 9.5% yield, whereas the 2,5-derivative 7b did not give detectable nitrene adduct. This experimental result indicates that the C$_3$- and C$_6$-bulky substituents of azepine ring are necessary for the additional nitrene reaction.[6] It was also observed that one-to-two adduct 5b was active to the nitrene to give 8b[11] and unidentified materials. This seems to be a reason for a low isolation yield of 5b in the reaction of nitrene with bis(trimethylsilyl)benzene.

Dehydrogenation and simultaneous desilylation were successfully carried out by the treatment with dichlorodicyanoquinone (DDQ). N,N-Dimethoxycarbonyl derivative (9,[12] mp 163-164°C) was directly obtained when 5b and DDQ were heated in a dichlorobenzene solution at 180°C. The hydrolysis and decarboxylation of 9 using methanolic KOH gave the target compound, 1,4-dihydropyrrolo[3,2-b]pyrrole 1, in high yield : colorless needles, mp 123-124°C (dec); $C_6H_6N_2$; m/e 106 (M$^+$, base) ; IR (KBr) 3380, 3100, 1480, 1469, 1461, 1340, 1300 cm^{-1} ; ^{1}H-NMR (90MHz, in CDCl$_3$) δ 6.05 (2H, m), 6.73 (2H, d of d), 7.52 (2H, NH) ; ^{13}C-NMR (22.6MHz, in acetone-d$_6$) δ 91.5 (d), 120.3 (d), 128.9 (s) ;

UV (in cyclohexane) λ max= 245 nm (ε= 14110).



5b 9 1

Product 1 is a parent compound of fundamental heterocyclic system possessing 10π-electrons, but it is labile and air-sensitive compared with the 3,6-di-tert-butyl derivative 1a. The pure crystals of 1 could be obtained by a sublimation followed by swift recrystallization from acetone-hexane, and they turned out to be unstable decomposing to blue material on standing in air at room temperature. The oxidation potential of 1 was measured with cyclic voltammetry to be 0.48 V (vs. SCE) in acetonitrile. This value is almost half in comparison with that of pyrrole and might cause the instability of dihydropyrrolo[3,2-b]pyrrole. A similarity in ^{1}H-NMR spectrum between pyrrolo[3,2-b]-pyrrole 1 and pyrrole indicates that same order of ring current and aromaticity are present in both ring systems. The faintly higher field shift (0.17 ppm) of β-proton in 1 observed seems to reflect the electron density of this system which is influenced by the adjacent pyrrole ring. In ^{13}C-NMR spectrum of 1, the deviation (16.7 ppm) from the chemical shift of pyrrole at β-position also suggests that an increase in electron density is due to the electron donating character of the adjacent nitrogen atom.

The synthesized pyrrolo[3,2-b]pyrrole 1 was unstable under acidic condition to give immediately polymeric material different from its di-tert-butyl derivative. Attempts to oxidize to 1,4-diazapentalene were unsuccessful under several conditions used for the case of 1a[13]. On the other hand, it was observed that the treatment of 1 with NaH afforded the dianion which was converted to the 1,4-dimethyl derivative by methyl iodide. Further investigations concerning the chemical and physical properties of 1 are in progress.

References

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2. V.P. Litvinov and Ya.L. Gol'dfarb, Advances in Heterocyclic Chem., 19, 123 (1976) and references cited therein.

3. Compound 2 was synthesized by Soth.[4] Although the 1,4-dimethyl derivative of 1 was inadvertently prepared by thermolysis of triazatrishomobenzene,[5] the parent compound 1 is still unknown. The chemistry of pyrrolopyrroles also remains ambiguous.
4. S. Soth, C. R. Acad. Sc Paris, 281, 793 (1975).
5. H. Prinzbach, R. Schwesinger, M. Breuninger, G. Gallenkamp, and D. Hunkler, Angew. Chem. Int. Ed. Engl., 14, 347 (1975).
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7. K. Satake, T. Kumagai, and T. Mukai, submitted to Chem. Lett., 1984.
8. Product 5b: colorless needles, $C_{16}H_{28}N_2O_4Si_2$; Mass m/e 368(M^+,12%), 353(base); IR(KBr) 3100, 3030, 2960, 2905, 1717, 1599 cm^{-1}; UV λmax= 224 (ε= 34800) nm in cyclohexane.
9. 3,6-Bis(trimethylsilyl)-1H-azepine 6b: pale yellow oil, $C_{14}H_{25}NO_2Si_2$; Mass m/e 295 (M^+,76%), 176(base); IR(oil) 3025, 2970, 2910, 1731, 1620, 1579 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 0.10(18H, s), 3.77(COOMe), 5.87(H_4 and H_5, s), 6.23 (H_2 and H_7, s); ^{13}C-NMR($CDCl_3$) δ -1.7(q), 52.9(q), 131.2(s), 132.6(d), 134.5(d), 154.3(s); UV λmax= 222 (ε= 19000), 257 (3600), 315 (580) nm in cyclohexane.

   2,5-Bis(trimethylsilyl)-1H-azepine 7b: pale yellow oil, $C_{14}H_{25}NO_2Si_2$; Mass m/e 295 (M^+,28%), 176(base); IR(oil) 3040, 3010, 2960, 2900, 1714, 1621, 1595 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 0.13(9H, s), 0.17(9H, s), 3.72(COOMe), 5.7-6.0 (2H, m), 6.10(1H, m), 6.53(H_7, d, J= 4.5Hz); UV λmax= 231 (ε= 19100), 333 (1280) nm in cyclohexane.
10. J.B. Lambert, H.F. Shurvell, L. Verbit, R.G. Cook, and G.H. Stout, "Organic Structural Analysis", pp 121, Macmillan Publishing Co. Inc., New York.
11. Product 8b: colorless needles, mp 160-161°C, $C_{15}H_{23}N_3O_6Si$; Mass m/e 369 (M^+,base); IR(KBr) 3360, 3180, 3110, 3015, 2960, 2905, 1733, 1705, 1589, 1540 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 0.15(9H, s), 3.70(COOMe), 3.72(COOMe), 3.80 (COOMe), 5.42(H_{3a} and H_{6a}, s), 6.48(H_5, splitted d), 6.95(H_2, br s), 7.78 (NH); ^{13}C-NMR($CDCl_3$) δ -1.3(q), 53.4(q), 53.5(q), 65.1(d), 66.3(d), 113.6 (d), 120.1(s), 120.7(s), 136.8(d), 153.3(s), 153.9(s); UV λmax= 233 (ε= 22370), 237 (22280), 265 (sh, 4000) nm in cyclohexane.
12. N,N-Dimethoxycarbonyl-1,4-dihydropyrrolo[3,2-b]pyrrole 9: colorless plates, mp 163-164°C, $C_{10}H_{10}N_2O_4$; Mass m/e 222(M^+,base); IR(KBr) 3170, 3150, 2960, 1740 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 4.00(6H, COOMe), 6.44(H_3 and H_6, d, J= 3.0Hz), 7.17(H_2 and H_5, d, J= 3.0Hz); ^{13}C-NMR($CDCl_3$) δ 54.0(q), 101.6(dd), 122.0 (dd), 127.5(s), 151.1(s); UV λmax= 250 (sh, ε= 8160), 256 (17100), 277 (9080), 282 (sh, 8930), 294 (sh, 5200) nm in cyclohexane.
13. K. Satake, T. Kumagai, S. Tanaka, and T. Mukai, to be submitted.

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