CHEMISTRY LETTERS, pp. 743-746, 1983. © The Chemical Society of Japan

# CHEMICAL BEHAVIOR AND PROPERTIES OF TETRAHYDROPYRROLO[3,2-b]PYRROLE$^{1)}$

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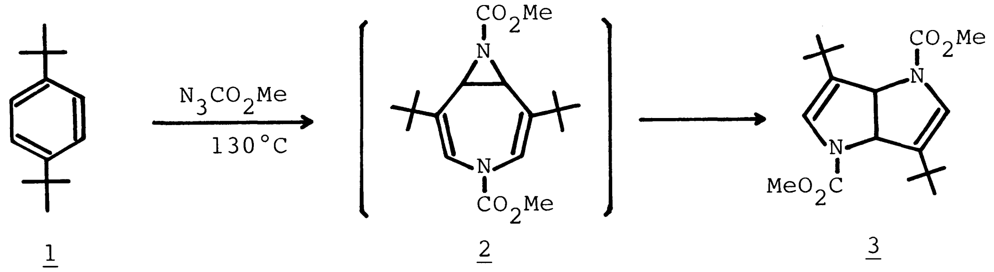
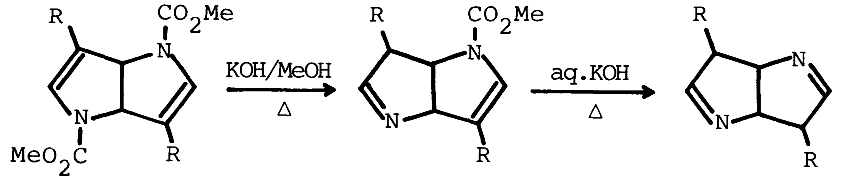
Upon treating under basic or acidic conditions, tetrahydropyrrolo-[3,2-b]pyrrole derivative 3 easily undergoes demethoxycarbonylation or ring-opening reactions affording bicyclic diimine 5 or pyrrole derivatives such as 10 and 12. In addition, dehydrogenation of 3 results in the formation of dihydropyrrolo[3,2-b]pyrrole derivative 13, which shows [4+2] cycloaddition reaction with dimethyl acetylene-dicarboxylate to give indole derivative 15.

In a previous paper,$^{2)}$ we reported a one-pot-synthesis of dimethyl 3,6-di-t-butyl-1,3a,4,6a-tetrahydropyrrolo[3,2-b]pyrrole-1,4-dicarboxylate (3) starting from 1,4-di-t-butylbenzene (1) by use of thermally generated nitrene. The overall reaction leading to bicyclic compound 3 involves the formation of 4,5-azahomo-1H-azepine (2) as an intermediate. We are interested in the chemical behavior of the bicyclic compound 3 because of the possibility of giving variety of heterocyclic compounds. Potent reactivities of 3 are due to the two ene-amide functional groups in its skeleton. In addition, we investigated the reaction of 1,4-dihydropyrrolo[3,2-b]pyrrole 13 which was derived from 3. Literatures on pyrrolo[3,2-b]pyrrole derivatives are only a few, except studies on 1,4-dimethyl and 1-methyl-2-methoxycarbonyl derivatives which have been synthesized by Prinzbach$^{3)}$ and Hemetsberger.$^{4)}$

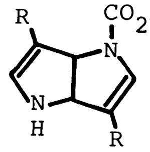


When 3 was treated with a methanolic KOH solution at a room temperature for 24 h, hydrolysis and subsequent decarboxylation occurred to give a yellow oil in 70 % yield. The structure was assigned as methyl 3,6-di-t-butyl-1,3a,6,6a-tetrahydropyrrolo[3,2-b]pyrrole-1-carboxylate (4) based on the following spectral data; Mass m/e 278 ($M^+$, 27 %); IR 1718, 1652, 1623 $cm^{-1}$; $^1H$-NMR (90 MHz, $CCl_4$) δ 1.02 (s, 9H), 1.19 (s, 9H), 2.94 (br s, 1H), 3.63 (s, 3H), 4.13 (d of d, J=7.5, 1.2 Hz, 1H), 4.93 (br d, J=7.5 Hz, 1H), 6.14 (br s, 1H), 7.32 (d of d, J=2.9, 1.2 Hz, 1H);

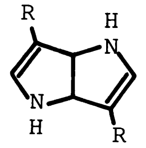
UV λmax (cyclohexane) 228 (ε 8,790), 287 (sh, 230) nm. When 4 was refluxed in a 0.5N-KOH aqueous solution for 12 h, further decarboxylation occurred and 3,6-di-t-butyl-3,3a,6,6a-tetrahydropyrrolo[3,2-b]pyrrole (5) was obtained in 85 % yield. The spectral properties are as follows; Mass m/e 220 (M$^+$, 17 %); IR 1623 cm$^{-1}$; $^1$H-NMR (90 MHz, CDCl$_3$) δ 1.05 (s, 18H), 2.71 (br s, 2H), 4.28 (br s, 2H), 7.42 (br s, 2H); UV λmax (cyclohexane) 233 (ε 1,580), 290 (1,055), 318 (sh, 150) nm. The IR and NMR spectra rule out the existence of the expected isomers, 4' and 5', which have enamine group instead of imine group. This result is compatible with the fact that $\Delta^2$-pyrroline is most stable among the isomers.[5)]



3 R= $^t$Bu 4 5



4'

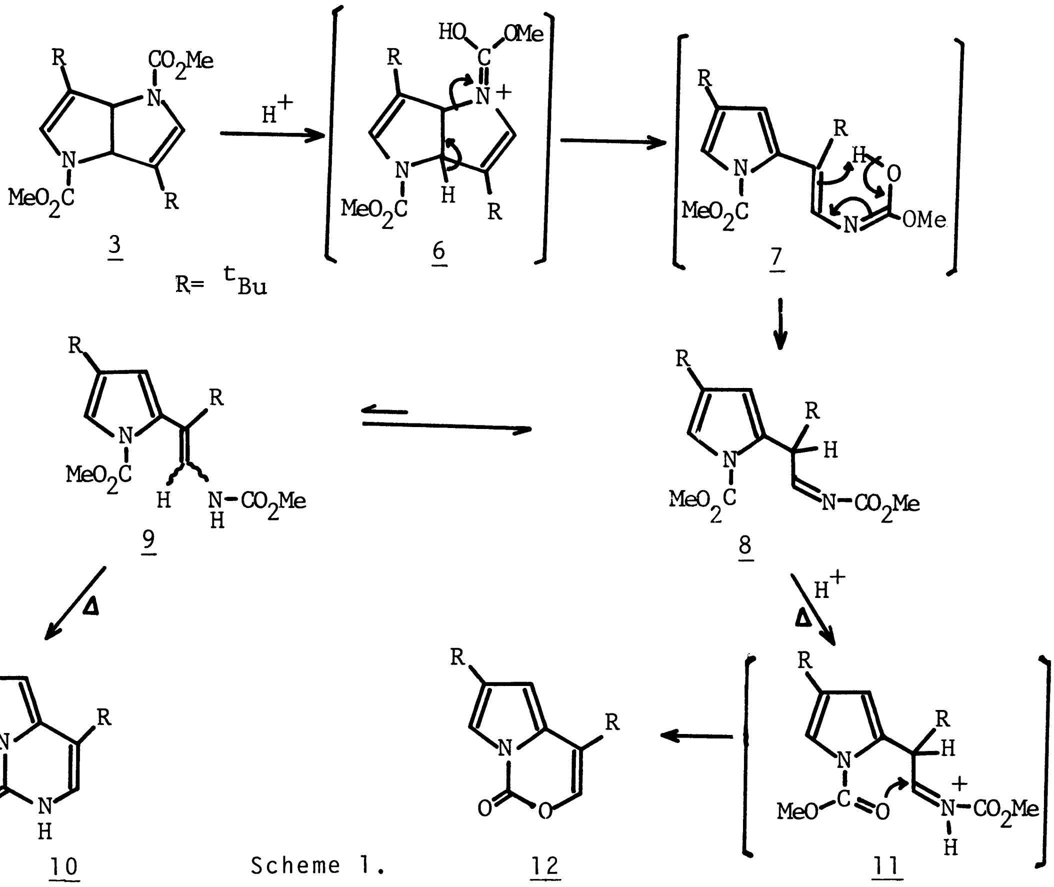


5'

On the other hand, ring opening reaction took place when 3 was heated in benzene containing p-toluenesulfonic acid as a catalyst at 80 °C for 2 h. Thus, 2-(2-pyrryl)-ethanimine derivative (8) was obtained in 98 % yield as a pale yellow oil. The structural assignment of 8 is based on the following spectral data; Mass m/e 336 (M$^+$, 70 %); IR 3440, 3325, 1758, 1740, 1699 cm$^{-1}$; $^1$H-NMR (90 MHz, CDCl$_3$) δ 1.05 (s, 9H), 1.24 (s, 9H), 3.66 (s, 3H), 3.38 (s, 3H), 5.92 (d, J=2.1 Hz, 1H), 5.97 (br d, J=10.8 Hz, 1H), 6.67 (br d, J=10.8 Hz, 1H), 7.04 (d, J=2.1 Hz, 1H), UV λmax (cyclohexane) 225 (ε 19,520), 250 (sh, 5,620) nm. The tautomeric isomer 9 could not be detected in the NMR spectrum but the IR spectrum (weak $\nu_{N-H}$ bands at 3440 and 3325 cm$^{-1}$) shows the existence of a small amount of 9.

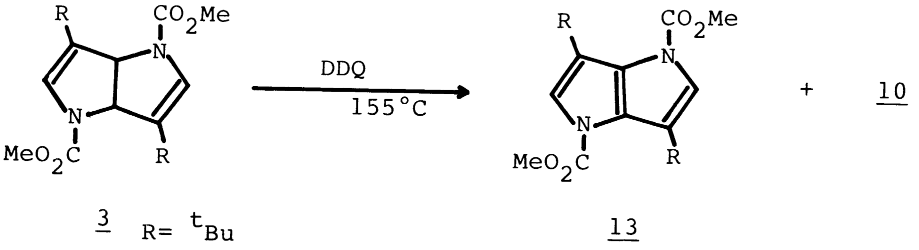
As shown in Scheme 1, the formation of 8 can be explained by protonation of 3 at an oxygen atom of the methoxycarbonyl group giving cationic species 6, followed by a ring opening reaction leading to pyrrole intermediate 7, which then undergoes proton migration to afford imine derivative 8 possessing pyrrole moiety.

When compound 8 was heated in bromobenzene at 160 °C for 3 h, 4,6-di-t-butyl-1,2-dihydropyrrolo[1,2-c]pyrimid-1-one (10), mp 204-205 °C, was obtained in 62 % yield. Heating of 8 in bromobenzene containing one equivalent of p-toluenesulfonic acid at 155 °C for 4 h produced 4,6-di-t-butyl-1H-pyrrolo[1,2-c][1,3]oxazin-1-one (12), mp 87-88 °C, in 82 % yield. The constitutions of 10 and 12 are deduced based on their spectral properties which are presented here; Mass m/e 246 (M$^+$, 100 %); IR 3300, 3220, 3100, 1725, 1686, 1625 cm$^{-1}$; $^1$H-NMR (90MHz, CDCl$_3$) δ 1.33 (s, 9H), 1.37 (s, 9H), 6.41 (d, J=1.8 Hz, 1H), 6.43 (d, J=4.8 Hz, 1H), 7.39 (d, J=1.8 Hz, 1H), 10.08 (br, 1H); UV λmax (EtOH) 277 (ε 10,930) nm for 10, and Mass m/e 247 (M$^+$, 54 %); IR 1755, 1645, 1622 cm$^{-1}$; $^1$H-NMR (90 MHz, CDCl$_3$) δ 1.32 (s, 9H), 1.37 (s, 9H), 6.48 (d, J=1.7 Hz, 1H), 6.77 (s, 1H), 7.36 (d, J=1.7 Hz, 1H); UV λmax (EtOH) 223 (ε 9,320), 228 (9,210), 271 (9,270) nm for 12. The formation of 10 and 12 can be accounted for as shown in Scheme 1 starting from 9 and 8, respectively. In the absence of acid, vinylurethane 9 undergoes cyclization and subsequent demethoxycarbonylation to give 10. Under acidic condition, imino-isomer 8 is protonated to give the iminum salt 11[6] which then converts to 12. To our knowledge, no report on pyrrolo[1,2-c][1,3]oxazine derivatives was found, although pyrrolo[1,2-c]pyrimidine derivatives have been studied by Rapopport.[7]



Scheme 1.

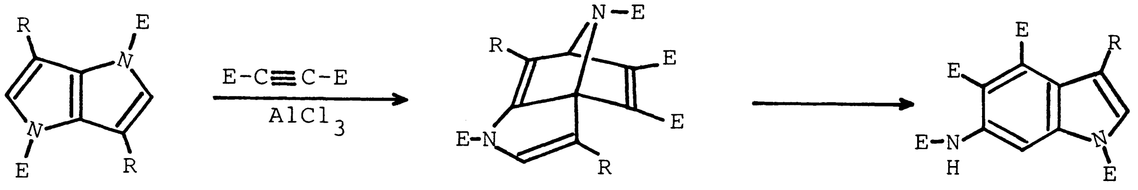
Dehydrogenation of 3 was carried out by heating with 1.2 molar equivalents of DDQ at 155 °C for 4 h, where dimethyl 1,4-dihydro-3,6-di-t-butyl-pyrrolo[3,2-b]-pyrrole-1,4-dicarboxylate (13), mp 240-241 °C, was obtained in 67 % yield,accompanied by 10 (27 % yield). The formation of by-product 10 is rationalized by the effect of a trace of acid formed in the reaction mixture. The structure of 13 is confirmed on the basis of following spectral data; Mass m/e 334 (M$^+$, 100 %); IR 1760, 1558, 1545 cm$^{-1}$; $^1$H-NMR (90 MHz, CDCl$_3$) δ 1.41 (s, 18H), 3.93 (s, 6H), 7.04 (s, 2H); $^{13}$C-NMR (50 MHz, CDCl$_3$) δ 121.1, 126.4, 128.3 (ring carbons):



δ 30.9, 31.8 (t-butyl): δ 151.0, 53.8 (COOMe); UV λmax (cyclohexane) 254 (ε 16,980), 262 (18,200), 283 (8,910) nm.

Dihydropyrrolopyrrole derivative 13 belongs to intriguing bicyclic system consisting of five-membered heterocycles which should attract much attention in connection with the aromatic character8) as well as the electronic effect of the nitrogen atoms of the cyclic π-system.9)

One of the interesting reactions of 13 is Lewis acid-catalyzed Diels-Alder reaction.10) When 13 and dimethyl acetylenedicarboxylate were heated in dichloromethane at 40 °C for 1 h in the presence of $AlCl_3$, methyl 6-methoxycarbonylamino-4,5-di-methoxycarbonyl-3-t-butylindole-1-carboxylate (15) was obtained as colorless prisms (mp 163-164 °C) in 83 % yield. The structure of 15 is confirmed by comparison with the spectral data of methyl indole-1-carboxylate11) and on the basis of following spectral data; Mass m/e 420 ($M^+$, 15 %); IR 3150, 1740, 1722, 1606 $cm^{-1}$; $^1H$-NMR (90 NHz, $CDCl_3$) δ 1.38 (s, 9H), 3.79 (s, 3H), 3.89 (s, 6H), 4.06 (s, 3H), 7.48 (s, 1H), 8.68 (s, 1H), 10.32 (br, 1H); UV λmax (EtOH) 249 (ε 20,400), 284 (6,000), 315(sh) nm. The formation of 15 could be explained by postulating an expected [4+2] cycloaddition affording 14 followed by a C-N bond cleavage and subsequent aromatization.



13 14 15

R= $^tBu$, E= COOMe

Further investigation of physical and chemical properties of pyrrolo[3,2-b]pyrrole derivative 13 will be published elsewhere.

## References

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(Received February 18, 1983)