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SYNTHESIS AND PROPERTIES OF 1,4-DIHYDROPYRROLO[3,2-b]-PYRROLE-2,5-DIONE DERIVATIVES

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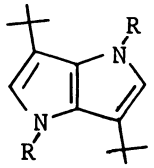
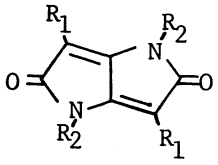
A new approach to 1,4-dihydropyrrolo[3,2-b]pyrrole-2,5-dione derivatives, which are regarded to belong to an interesting redox system, is described. Reduction potentials along with chemical and spectral properties of these derivatives are presented, and the capability as electron acceptors is also discussed.

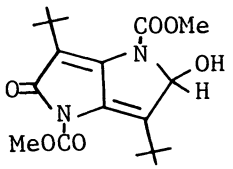
In a previous paper, it was pointed out that 3,6-di-t-butyl-1,4-dihydropyrrolo[3,2-b]pyrrole derivatives (1) belong to a bicyclic 10π-electron system and that they are more electron rich and more basic than pyrrole and indole.[1] Recently we found that the N-carbomethoxy derivative (1b) is efficiently oxidized to the corresponding 2,5-dione (2b) which can then be converted into the free imino derivative (2a). This bicyclic lactam which contains diene-dione and enamine functions is expected to attract much attention because of its structural similarity to the biochemically important oxidants such as flavins[2a] and quinoproteins.[2b] In addition, such heterocyclic diene-dione derivatives may be regarded as a new model for the Wurster-type redox system.[3] In spite of their simple fundamental structure and expected intriguing properties, only two derivatives are hither-to-known in the literature,[4,5] and no description on their properties is presented. We wish to report a new synthetic approach to this system as well as chemical and spectral properties including the reduction potentials of the newly synthesized compounds (2a-c) and previously reported compound (2d).[4]



1a: R=H
1b: R=CO_2Me



2a: $R_1={}^tBu$, R_2=H
2b: $R_1={}^tBu$, $R_2=CO_2Me$
2c: $R_1={}^tBu$, R_2=Me
2d: R_1=H, R_2=Ph



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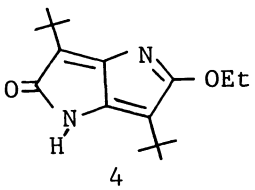

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When 1,4-dihydropyrrolo[3,2-b]pyrrole (1b) was treated with 2 equiv. of N-bromosuccinimide (NBS) in dioxane containing 1% water for 1 h at room temperature, an oxidized product (3)[6] was produced in 90% yield. The oxidation must be ascribed to bromine cation under these conditions.[7] The structure determination of 3 was based on its spectral properties.[6] Upon treating 3 with 2 equiv. of NBS under the similar conditions, the desired bicyclic lactam (2b)[8] was isolated in 86% yield. One-step oxidation of 1b to 2b could also be attained when 4 equiv. of NBS was applied. The spectral data,[8] especially the symmetrical appearance of ^{1}H and ^{13}C-NMR spectra, are compatible with the structure of 2b. Demethoxycarbonylation of 2b, to give 3,6-di-t-butyl-2,5-dioxo-1,4-dihydropyrrolo[3,2-b]pyrrole (2a)[9] could be achieved by refluxing in a 10% KOH-methanol solution in excellent yield (82%). The structure of 2a was also deduced by its spectral data.[9]

The free imino compound (2a) was isolated as stable yellow crystals sublimed easily which have high mp and poor solubility in water and common organic solvents. When the dianion derived from 2a (by treating with NaH) was refluxed with CH_3I in dioxane for 3 h, an N,N'-dimethyl derivative (2c)[10] was formed in 80% yield. In order to obtain 3,6-di-t-butyl-2,5-diethoxy-1,4-diazapentalene, an attempted O-alkylation was carried out by refluxing 2a with 10 equiv. of triethyloxonium tetrafluoroborate in methylene chloride for 15 h. However, the desired product was not formed, but instead 2-oxo-5-ethoxy-1,2-dihydropyrrolo[3,2-b]pyrrole (4)[11] was produced. Upon treating with water even at room temperature, 4 was easily hydrolyzed to regenerate 2a.

Electronic spectra of the 2,5-dioxo derivatives (2a-c) and N-phenyl derivative (2d) are shown in Fig. 1. They exhibit similar absorption curves, in which two absorption maxima are observed around 290 nm and around 350-450 nm. The latter band shows a red shift when an electron-donating group is introduced at the nitrogen atom. Based on MO (MNDO) calculation,[12] both HOMO and next HOMO are assigned to the π-orbitals, while the n-orbitals of the oxo groups are expected to be in lower levels. Therefore the above absorption maxima may originate from π-π^* excitation.

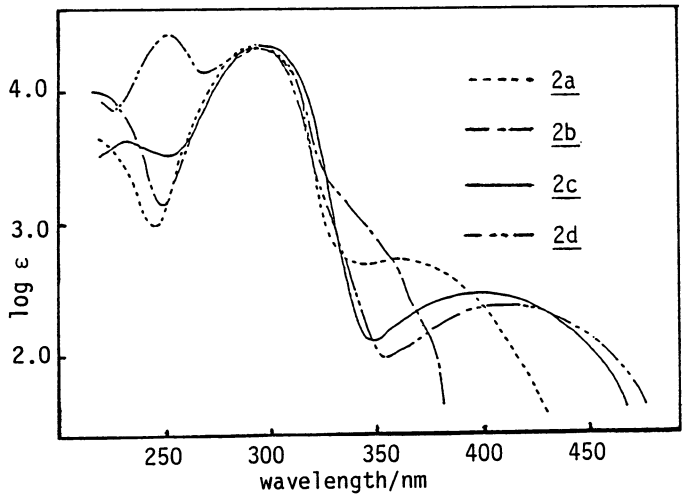
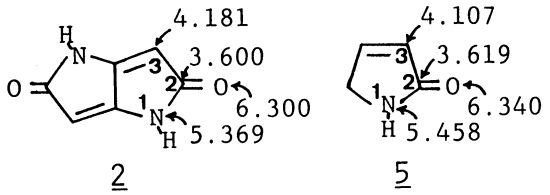


Fig. 1. The electronic spectra of (2a-d) in CH_3CN.

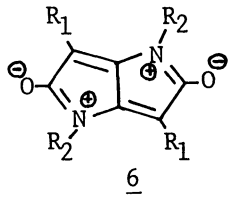


2 5

Fig. 2. Calculated charge densities.

Table 1. The carbonyl stretching bands and the ^{13}C chemical shifts of 2a-d and 5

Compound	2a	2b	2c	2d	5[a]
$\tilde{\nu}_{C=O}/cm^{-1}$	1714	1740 1803	1711	1720 1731	1675
C_3, δ/ppm	111.7	120.9	113.1	——[b]	127.6



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a) Ref. 13.

b) No data in Ref. 4.

In the IR spectra, carbonyl stretching bands of the bicyclic lactams (2a-d) appear at higher frequency region by 35 cm^{-1} compared with that of the related monocyclic analogue, 3-pyrrolin-2-one (5) (see Table 1). This suggests that polarization of the carbonyl group is smaller in 2a-d than in 5. The ^{13}C chemical shift at C-3 position is higher in 2a-c than in 5 as shown in Table 1. These characters are compatible with the charge density (calculated by MNDO[12]) on 2 and 5. As shown in Fig. 2 charge density at the carbonyl oxygen is smaller in 2 than in 5, whereas that at the C-3 position becomes larger in 2 than in 5. These facts might be rationalized by assuming that polarized structure (6) less contributes to the resonance because of its 8π-electron contribution.

The reduction potentials of 2a to 2d were measured by cyclic voltammetry and are listed in Table 2. The values suggest that bicyclic lactams (2a-d) are weaker electron acceptors compared with aromatic quinones because electron donating imino groups exist. However, except for free imino compound (2a) cyclic voltamgrams of 2b-d exhibit reversible redox curves, suggesting the formation of a stable anion radical 2^- and a dianion 2^{2-}. The semiquinone formation constants (K_{sem})[3a] of 2b and 2d which are considered as an index of the stability of the anion radicals are also shown in Table 2. Such large values stand for a great deal of the stabilty of anion radicals 2^-. An ESR study of the 10π-electron anion radicals 2^- is in progress.

Table 2. Reduction potentials (vs SCE) and K_{sem} of 2a-2d and the related quinone

Compound	2a	2b	2c	2d	*p*-Benzoquinone[c]
$E_{\frac{1}{2}}^{RED}$[a] /V	-1.17[b]	-1.20 -1.75	-1.59 <-2.0	-1.19 -1.72	-0.51 -1.17
K_{sem}	——	2.1×10^9	——	9.6×10^8	1.5×10^{11}

a) Measured by cyclic voltammetry using Pt-electrode in 0.10 mol/dm^3 $(NEt_4)ClO_4/CH_3CN$.

b) Irreversible.

c) Ref. 14.

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6) Product 3: colorless columns, mp 199-200 °C; Mass m/e 366 (M^+, 75%); IR (KBr) 3440, 2960, 1780, 1745, 1620 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 1.30 (s, 9H), 1.32 (s, 9H), 3.83 (d, J= 5.7 Hz, 1H), 3.86 (s, 3H), 3.93 (s, 3H), 6.12 (d, J= 5.7 Hz, 1H).

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8) Compound 2b: colorless columns, mp 144-145 °C; Mass m/e 364 (M^+, 74%), 349 (base); IR (KBr) 1803, 1740, 1648 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 1.33 (s, 18H), 3.97 (s, 6H); ^{13}C-NMR (22.5 MHz, $CDCl_3$) δ 28.3 (q), 33.0 (s), 54.8 (q), 120.9 (s), 143.6 (s), 151.1 (s), 167.8 (s); UV λ_{max}= 293 (ε= 20600) nm in ethanol.

9) Compound 2a: yellow columns, mp >340 °C; Mass m/e 248 (M^+, 18%), 233 (base); IR (KBr) 3220, 3050, 1714, 1660, 1651 cm^{-1}; ^{1}H-NMR (90 MHz, DMSO-d_6) δ 1.20 (s, 18H), 9.63 (s, 2H); ^{13}C-NMR (22.5 MHz, DMSO-d_6) δ 28.9 (q), 30.8 (s), 111.7 (s), 143.9 (s), 173.6 (s); UV λ_{max}= 293 (ε= 22340), 360 (520) nm in acetonitrile.

10) Compound 2c: yellow plates, mp 160.5-161.5 °C; Mass m/e 276 (M^+, 21%), 261 (base); IR (KBr) 2970, 1711, 1628 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 1.39 (s, 18H), 3.22 (s, 6H); ^{13}C-NMR (22.5 MHz, $CDCl_3$) δ 30.9 (q), 31.2 (q), 32.0 (s), 113.1 (s), 146.3 (s), 173.0 (s); UV λ_{max}= 296 (ε= 22000), 397 (286) nm in acetonitrile.

11) Product 4: orange columns, mp 159-160 °C; Mass m/e 276 (M^+, 35), 261 (base); IR (KBr) 3220, 2970, 1722, 1684, 1655 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 1.23 (s, 9H), 1.28 (s, 9H), 1.41 (t, J= 7.2 Hz, 3H), 4.45 (q, J= 7.2 Hz, 2H), 8.58 (s, 1H).

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