The synthesis and studies of heterocyclic quinones were important in conjunction with bioreductive alklylation and the design of new alkylating agents. The reductive alkylating agents are quinones functionalized with leaving groups so as to permit quinone methide formation upon reduction.\(^1\)\(^–\)\(^3\) Reported here is the synthesis of pyrrolo[1,2-a]benzimidazole-5,8-diones and its reduced analogues as model of potential reductive alkylating agents. Although many pyrrolo[1,2-a]benzimidazole have been synthesized\(^6\)\(^–\)\(^8\) and studied since 1955, there was only one report for the synthesis of pyrrolo[1,2-a]benzimidazoles bearing quinone moiety.\(^3\) Such derivatives may exhibit quinone mediated reactions such as reductive alklylation and redox reaction. We found that 6 was conveniently converted to 7 upon treatment with concentrated hydrobromic acid, which indicate that 6 possesses very high reduction potential.\(^5\) The synthetic sequence described in Scheme 1 may be a versatile route to these novel pyrrolo[1,2-a]benzimidazole based heterocyclic quinone systems. A. R. Freeman and coworkers have prepared various pyrrolo[1,2-a]benzimidazole by annelation of the benzimidazole and pyrrole rings with an appropriately substituted benzene.\(^4\) Unfortunately, such benzene derivatives are not always available which could be easily converted to a benzoquinone to ring annelation. We have attempted the preparation of 6 starting from 2-amino-4-chlorotoluene. The reaction sequence leading to 6 and 7 is shown in Scheme 1. As is shown, the synthesis relies on the formation of 2 which could be cyclized to the pyrrolo[1,2-a]benzimidazole 3. Treatment of 2-amino-4-chlorotoluene with neat pyrrolidine at reflux resulted substitution product 1 as well as amide hydrolysisis product. The ratio of the two products was 50/50 in this reaction. Subsequent catalytic hydrogenation of the mixture to reduce nitro group followed by treatment with acetic anhydride afforded 2 as the sole product. The \(^1\)H-NMR spectrum of 2 in DMSO-\(d_6\) shows three different methyl groups indicating peracylationation of reduced form of 1. Cyclization of 2 to pyrrolo[1,2-a]benzimidazole 3 was accomplished by two different methods. Not only cyclization of 3 in the presence of performic acid gave desired product 4 but also thermal reaction in boiling \(n\)-butanol also gave desired product. The former cyclization is thought to involve \(t\)-amine N-oxide followed by acetyl transfer to N-oxide and subsequent elimination of acetyl group to give iminium ion which was then cyclized and oxidized.\(^6\) The latter cyclization is thought involve[1,5]-sigmatropic H-shift.\(^9\) The rate of reaction monitored by UV-Vis spectrometer seemed to depend on the substrate concentration. Detailed kinetic studies are under progress. Nitration of 3 proceeded...
smoothly to afford mononitrated product 4 regio-
selectively, which gave amino product 5 after cat-
ytic reduction.

Treatment of 5 with refluxing formic acid afforded
6 indicating that original nitration occurred at
8-position of 3. Cyclization of 5 to 6 was evidenced
by $^1$H-NMR and IR spectroscopy. IR spectrum
clearly shows that there is no absorbance
attributed to carbonyl stretching of 5. Far down-
field shift of N-H proton from 8.87 to 8.230
indicate that N-H proton in the imidazole moiety
has intramolecular hydrogen bonding. Only one
tautomeric form was isolated in this reaction.
Treatment of 5 with Fremy's salt in pH 3 aqueous
phosphate buffer provided quinone 6. The struct-
tural data are as follows: mp: 219~220°C; IR
(KBr, cm$^{-1}$) 3240(s), 1651(s), 1510(s); $^1$H-NMR
(DMSO-d$_6$) $\delta$ 9.54 (1H, s, amide-H), 4.14 (2H, t, J=
7.0 Hz, C(1)-methylene), 2.85 (2H, t, J=7.0 Hz,
C(3)-methylene), 2.60 (2H, quint, J=6.4 Hz, C(2)-
methylene), 2.05 (3H, s, 6-methyl), 1.83 (3H, s,
acetyl).

Hydroquinone 7 was obtained by catalytic reduc-
ton of 6 in methanol. The compound 7 was
air stable and obtained as hydrochlorids salt. The
distinctive feature of hydroquinone was seen in $^1$H-
NMR spectrum. The structural data for 7 are as
follows: IR (KBr, cm$^{-1}$) 3380(s), 3140(s), 1660(s),
1490(s), 1290(m); $^1$H-NMR (DMSO-d$_6$) $\delta$ 9.46 (1H,
s, amide-H), 9.43 and 9.21 (2H, 2s, two Ar-OHs,
no assignment made), 4.44 (2H, quint, J=4.7 Hz,
C(2)-methylene), 2.50 (3H, s, 7-methyl), 2.10 (3H,
s, acetyl).

Various attempt to introduce leaving groups at
3-position of 6 resulted in different products. As
shown in Scheme 2, attempted allylic bromination
of 6 with N-bromosuccinimide (NBS) gave 10.
This result indicates that benzylic bromination is
more favorable than allylic bromination in 6.
When 5 was treated with NBS, 9 was formed quan-
titatively. Cyclization of acetamido group and
aromatic bromination were evidenced by $^1$H-NMR
and IR spectra. $^1$H-NMR (CDCl$_3$) spectrum of 9
shows disappearance of aromatic proton and IR
spectrum clearly shows that there is no absorbance
attributed to carbonyl stretching of 5. Also
only one tautomeric form of imidazole ring was
isolated in this reaction. Treatment of 6 with NBS
afforded 10 as sole product which was slowly de-
composed in air. This hydroquinone could elimi-
nate HBr to afford orthoquinone methide, which
traps nucleophiles. Currently we are trying to
characterize possible intermediates in this reaction.

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11. 1H-NMR (DMSO-d6, TMS) 6 12.23 (1H, s, N-H), 7.09 (1H, s, Ar-H), 4.29 (2H, t, J = 8.0 Hz, C(1)-methylene), 2.92 (2H, t, J = 8.0 Hz, C(3)-methylene), 2.65 (2H, quint, J = 8.0 Hz, C(2)-methylene), 2.53 and 2.50 (6H, 2-6, 6 and 8-methyls, no assignment made).
12. 1H-NMR (DMSO-d6) 6 9.46 (1H, s, N-H), 9.43 and 9.23 (2Hs, two s, Ar-OHs, no assignment made), 4.44 (2H, t, J = 6.8 Hz, C(2)-methylene), 3.25 (2H, t, J = 6.8 Hz, C(3)-methylene), 2.73 (2H, quint, J = 6.8 Hz, C(2)-methylene), 2.09 and 2.11 (6H, two s, methyls, no assignment made).
13. 1H-NMR (CDCl3) 6 4.32 (2H, t, J = 6.0 Hz, C(1)-methylene), 3.07 (2H, t, J = 6.0 Hz, C(3)-methylene), 2.78 (2H, quint, J = 6.0 Hz, C(2)-methylene), 2.20 and 1.67 (6H, two s, methyls, no assignment made).