

PREPARATION OF *p*-BENZOQUINONO[*b*]OXEPINES AND THEIR AROMATIC RING ANNULATED DERIVATIVES

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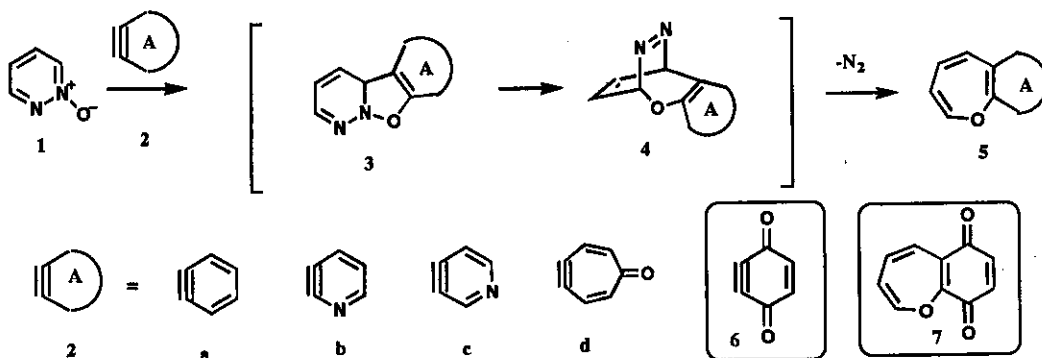
Abstract - Reaction of pyridazine *N*-oxides with 2,3-didehydrobenzoquinone resulted in the formation of the novel *p*-benzoquinono[*b*]oxepines, from which their aromatic ring annulated derivatives such as naphthoquinono-, anthraquinono-, 1-azanaphthoquinono-oxepines were prepared by Diels-Alder reactions.

Fully unsaturated monocyclic oxepines are well known to be thermally unstable because of their non-aromatic character due to 8π -electron system and benzene oxide-oxepine equilibrium. Extensive studies on the heteroepines revealed that the stability of oxepine ring could be enhanced by introduction of electron-withdrawing or bulky substituents on the ring, or by condensation with benzene rings.¹

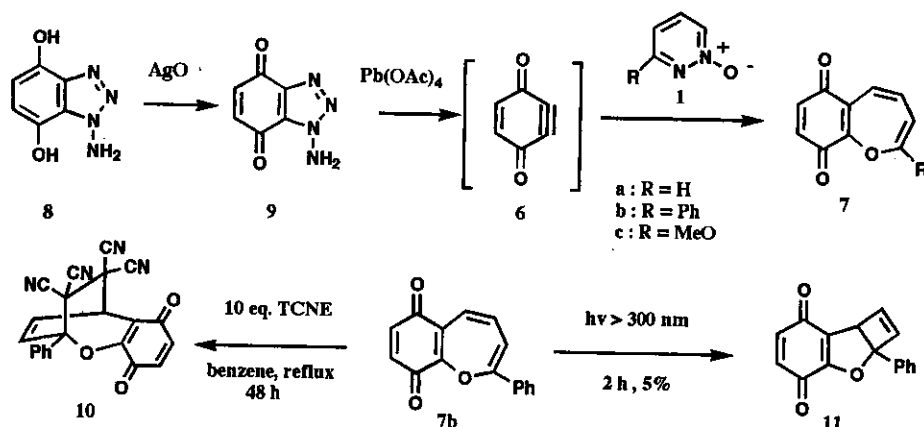
Therefore, we were interested in the syntheses and properties of the fused oxepines condensed with various highly electron deficient rings.

We have previously found that the 1,3-dipolar cycloadducts (3), formed by the reaction of the pyridazine *N*-oxides (1) with benzyne (2a), spontaneously eliminated N_2 to give the 1-benzoxepine (5a) via the 1,3-rearrangement intermediates (4).² This method enabled us not only to prepare 1-benzoxepines in large scales as well as in one step, but also to offer an attractive route to novel classes of fused oxepines such as pyrido-(5b,c)³ and tropono-oxepines (5d)⁴ by using corresponding arynes (2b-d).

As an extension of our studies, we now communicate the preparation of benzoquinono[*b*]oxepines(7), by employing pyridazine *N*-oxides (1) and 2,3-didehydro-*p*-benzoquinone (6), and the results of some reactions concerning this novel ring system.



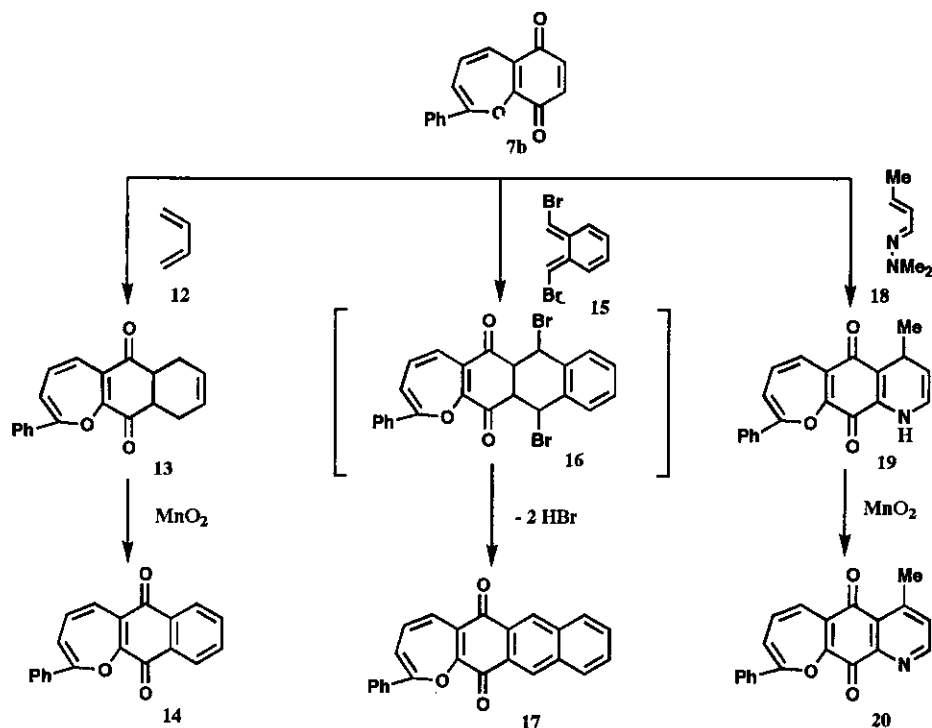
We used Rees's compound,⁵ 1-amino-4,7-dihydroxybenzotriazole (**8**), as the precursor for 2,3-didehydro-*p*-benzoquinone (**6**). The triazole (**8**) was converted to 1-aminobenzotriazole-4,7-quinone (**9**) by treatment with silver oxide in THF containing anhydrous sodium sulfate. The quinone (**9**) was rapidly oxidized with $\text{Pb}(\text{OAc})_4$ in CH_2Cl_2 at 0 °C to generate didehydrobenzoquinone (**6**), which was trapped *in situ* with a large excess of pyridazine *N*-oxides (**1 a-c**) to afford the expected *p*-benzoquinono[*b*]oxepines (**7 a-c**)⁶ in 10~20% yields based on the aminotriazole (**8**), as the sole isolable products.



The *p*-benzoquinono[*b*]oxepines (**7**) thus obtained are stable violet crystallines and in the ^1H -nmr spectra, almost all oxepine ring protons of **7** resonated at lower fields than those of 1-benzoxepine,⁷ indicating that the electron density of the oxepine ring of **7** is decreased by the highly electron deficient *p*-benzoquinone ring and thus the stability of **7** is increased. This tendency of lower electron density on the oxepine ring was also reflected on the decreased reactivities of **7** as active dienes. For example, the [4+2] π cycloaddition of **7b** with tetracyanoethylene (TCNE) proceeded only in refluxing benzene for a long time (48 h or more) and, upon irradiation, the intramolecular [2+2] π cycloadduct (**11**) was obtained only in a poor yield (*ca.* 5%). 1-Benzoxepines are known to readily react as dienes with a variety of dienophiles under milder conditions⁸ and undergo photo-induced intramolecular cyclization to afford the corresponding products in high yields.⁹

Many quinone derivatives are known to have important biological activities. That urged us to synthesize some polycyclic quinonoxepines by using Diels-Alder reaction of **7** with dienes.

Reaction of **7b** with butadiene (**12**) in CHCl_3 at -10°C for 7 days gave the adduct (**13**) in quantitative yield, which was readily oxidized with MnO_2 in refluxing benzene to the naphthoquinonoxepine (**14**)¹⁰ in 90% yield. *o*-Quinodimethane derivative (**15**)¹¹ also reacted smoothly with **7b** to give the anthraquinonoxepine (**17**)¹⁰ in 25% yield in one step *via* the initially formed adduct (**16**). Furthermore, the reaction of **7b** with 1-azadiene derivative (**18**)¹² proceeded regioselectively to form the compound (**19**) in 76% yield, which was led to the pyridoquinone ring fused oxepine (**20**)¹⁰ in 89% yield. The structure of **20** was confirmed by X-ray crystallographic analysis.¹³ The reason why only one regioisomer was obtained in this reaction with the 1-azadiene is not clear at present.



REFERENCES AND NOTES

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6. p-Benzoquinono[b]oxepine (7a): 10% yield, deep violet needles (from hexane), mp 85–86.5 °C, ms (m/z): 174 (M^+), ir (KBr) cm^{-1} : 1662 (C=O). *Anal.* Calcd for $C_{10}H_6O_3$: C, 68.97; H, 3.47. Found: C, 69.02; H, 3.49. 1H -Nmr ($CDCl_3$) δ : 5.80 (1H, dd, $J_{2,3} = J_{3,4} = 5.90$ Hz, 3-H), 6.08 (1H, d, $J_{2,3}$

= 5.90 Hz, 2-H), 6.61 (1H, dd, $J_{3,4} = 5.90$ Hz, $J_{4,5} = 11.00$ Hz, 4-H), 6.76 (1H, d, $J_{7,8} = 9.90$ Hz, 7-H), 6.81 (1H, d, $J_{7,8} = 9.90$ Hz, 8-H), 6.87 (1H, d, $J_{4,5} = 11.00$ Hz, 5-H). ^{13}C -Nmr (CDCl_3) δ : 186.6 (s, 6-C), 181.8 (s, 9-C), 145.7 (s, 9a-C), 130.8 (s, 5a-C), 143.0 (d, 2-C), 136.1 (d, 8-C), 135.9 (d, 7-C), 135.3 (d, 4-C), 125.6 (d, 5-C), 118.3 (d, 3-C).

2-Phenyl-*p*-benzoquinono[*b*]oxepine (**7b**): 20% yield, mp 127~128 °C.

2-Methoxy-*p*-benzoquinono[*b*]oxepine (**7c**): 15% yield, mp 101.5~103 °C.

7. The values of the chemical shifts of the ring protons of 1-benzoxepine are reported in ref. 2. [δ : 6.14 (2-H), 5.35 (3-H), 5.93 (4-H), 6.54 (5-H).]

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10. **14**: mp 184~186 °C; **17**: mp 240~242 °C; **20**: mp 179~181 °C.

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