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THE ACID CATALYZED CYCLIZATION OF 1,4-DIAMINO-2-β-HYDROXYETHYLAMINOANTHRAQUINONES: A SYNTHESIS OF THE ANTHRA[1,2-b]-1,4-OXAZINE-DIONE SYSTEM

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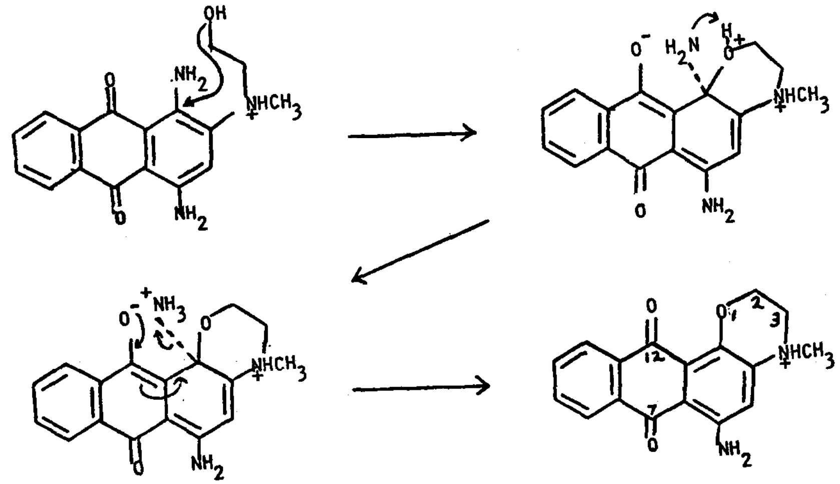
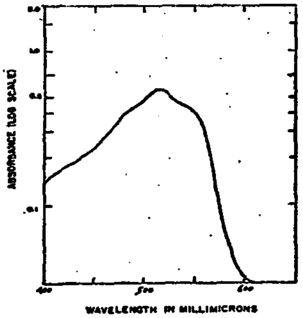
In a recent communication (1) we described the formation of 1,4-diamino-2-(N-alkyl-β-hydroxyethylamino)anthraquinones by a Smiles rearrangement of 1,4-diamino-2-(β-alkylaminoethoxy)anthraquinones. We now report a remarkably facile transformation of these 1,2,4-triaminoanthraquinones which leads to what we believe is the first preparation of the 4-H-anthra[1,2-b]-1,4-oxazine ring system. We interpret the reaction as proceeding by this sequence:

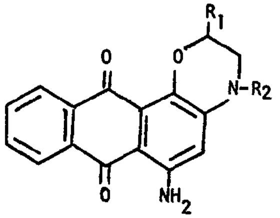


When an acetone solution of 1,4-diamino-2-(N-methyl-β-hydroxyethylamino)anthraquinone is stirred with 10% aqueous hydrochloric acid at 50° the red-violet solution clouds and an orange hydrochloride salt precipitates. Neutralization and crystallization from methanol affords stout brown crystals analyzing for $C_{17}H_{14}N_2O_3$. The structure is reasoned from these considerations: 1. The loss of a molecule of ammonia is indicated by the empirical formula. 2. The visible spectrum (Figure) no longer shows the double peak characteristic of the 1,4-diaminoanthraquinone system. 3. The infra-red spectrum (KBr disk) shows a carbonyl band at 1670 cm^{-1} in the hydrochloride salt, shifting to 1640 cm^{-1} in the free base. This is additional evidence that the 1,4-diaminoanthraquinone system, in which both carbonyl frequencies are below 1625cm^{-1} (2), is no longer present. Disappearance of the 1,4-diamino system with concurrent loss of ammonia can be fully rationalized by the proposed cyclization to yield the oxazine ring. The NMR spectrum is in agreement with this structure.



δ(TMS)	Multiplicity	Protons	Assignment
2.94	singlet	3	N-CH_3
3.46	triplet(J=5.0)	2	3-CH_2
4.22	triplet(J=5.0)	2	2-CH_2
6.22	singlet	1	5-CH
7.6-7.9	multiplet	6{~2	9,10 =CH-CH=
7.9-8.25	multiplet	~4 (2 exch.)	8,11 CH's 6-NH_2

Other 1,4,-diamino-2-(N-alkyl-β-hydroxyethylamino)anthraquinones react in analogous fashion to give the expected products. Data are summarized in the following table.



6-Amino-2-R_1-4-R_2-2,3,7,12-tetrahydroanthra[1,2-b]-1,4-oxazine-7,12-diones

R_1	R_2	M.P.(°)	λ_{max}(mμ)	ε	Solvent
H	CH_3	296-6.5	514	11,200	isopropanol
			sho.550	8,200	
H	$HOCH_2CH_2$	258-9	517	10,600	isopropanol
			sho.555	8,000	
CH_3	$HOCH(CH_3)CH_2$	200-1	520	12,000	isopropanol
			sho.550	9,600	

1. M.S.Simon and J.F.Downey,Jr., Tetrahedron Letters, (1974)
2. B.E.Zaitsev, L.B.Preobrazhenskaya, B.N.Kolokolov, V.M.Allenov; Russian Journal of Physical Chemistry, 44, 1210 (1970) and references cited therein.