Deuterium Studies in the Disproportionation of Pyrimido[4,5-*b*]quinolinium Salts

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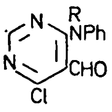
Summary Treatment of 4-chloro-6-*N*-alkylanilino-5-formylpyrimidines (**1**) with ethanolic hydrochloric acid gave high yields of 10-alkyl-pyrimido[4,5-*b*]quinolinium-4(3*H*)-ones (**2**; R^2 = H) which, at pH 9, underwent disproportionation to corresponding 10-alkyl-5,10-dihydropyrimido[4,5-*b*]quinolin-4(3*H*)-ones (**3**) and 10-alkyl pyrimido[4,5-*b*]quinolin-4,5(3*H*,10*H*)-diones (**4**); disproportionation of a 5-deuterio-salt (**6**) gave a 10-alkyl-5,5-dideuteriopyrimido[4,5-*b*]quinoline showing that the reaction involved hydride (deuteride) transfer from the 5-position of one molecule to the 5-position of another.

10-ALKYL-3,4-DIHYDRO-4-OXOPYRIMIDO[4,5-*b*]QUINOLINIUM salts (**2**; R^1 = Me or Et, R^2 = H, X = Cl) were obtained in high yields when the *N*-ethylanilinopyrimidine (**1**; R = Et) and its *N*-methylanilino analogue (**1**; R = Me) were treated with cold ethanolic hydrogen chloride. The salts (pK_a *ca.* 6·1) were fairly stable in cold or hot aqueous hydrochloric acid but when the pH was raised to about 8–9 each salt underwent rapid disproportionation at 20° to give a 10-alkyl pyrimidoquinolinone (**3**; R^1 = Et or Me, R^2 = H) and the corresponding dione (**4**; R^2 = H). A closely related 10-unsubstituted salt (**2**; R^1 = R^2 = H, X = Cl)[1] was stable in acid and alkali.



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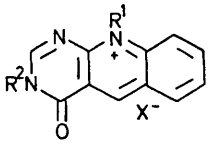

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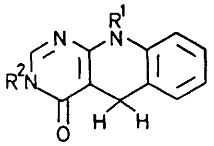

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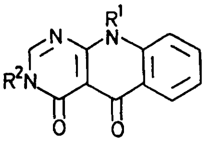

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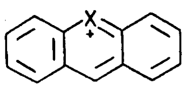

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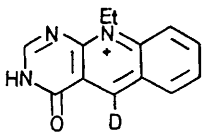

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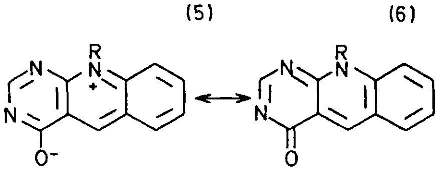

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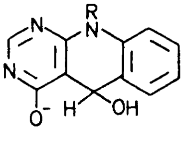

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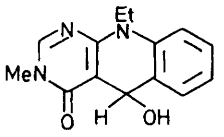

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The 10-ethyl-5,10-dihydro-compound (**3**; R^1 = Et, R^2 = H) was oxidised by permanganate to the 5-one (**4**; R^1 = Et, R^2 = H) and both the dihydro-compound and the 5-one underwent methylation at position 3. One of the resulting methyl compounds (**3**; R^1 = R_2 = Me) was oxidised by triphenylmethyl perchlorate to the aromatic pyrimidoquinolinium perchlorate (**2**; R^1 = Et, R^2 = Me, X = ClO_4) (pK_a 8·31) which also underwent disproportionation at about pH 9.

The disproportionations were shown to involve a hydride ion transfer from the 5-position of one molecule to the 5-position of another. When the *N*-ethylpyrimidoquinolinium salt (**2**; R^1 = Et, R^2 = H, X = Cl) was dissolved in deuterium oxide and the solution was adjusted to pH 9 with sodium deuteroxide the dihydropyrimidoquinoline formed (**3**; R^1 = Et, R^2 = H) contained no deuterium at position 5. Furthermore the 5-deuteriated salt (**6**), which was made from the 5-deuterioformyl analogue of the pyrimidine (**1**), underwent disproportionation in water and sodium hydroxide to give isotopically pure 10-ethyl-5,5-dideuteriopyrimido[4,5-*b*]quinolin-4(3*H*)-one and, of course, the corresponding 5-one.

The precise species involved in the present reactions have not yet been established but the fact that the pyrimidoquinolinium salts are stable in acid solution suggests that the cations (**2**) alone do not undergo disproportionation. Measurements of pK_a values and u.v. spectra indicate that the major species which are present under conditions where disproportionation is rapid include, in the 3-unsubstituted compounds, the zwitterion or neutral molecule (**7**) and its pseudo-base anion (**8**) and, in the 3-methyl compound, the salt (**2**; R^1 = Et, R^2 = Me) and its pseudo base (**9**). It is possible that hydride ion transfer occurs from a species such as (**8**) or (**9**) to one such as (**2**) or (**7**).

The reactions discussed resemble those of acridinium (**5**; X = NR),[2] xanthylium (**5**; X = O),[3] thioxanthylium (**5**; X = S),[4] and other similar salts[5] and have features in common with other disproportionations.[6,7] They are therefore representative of important and general reactions and are particularly suitable for further study because of the very mild conditions involved. Hydride ion transfers in related disproportionations have been suggested (*e.g.* ref. 6) but not proved by isotopic labelling. The present results, therefore, have significance in several fields of heterocyclic chemistry.

Structures of all compounds discussed have been established by microanalysis and ^1H n.m.r. spectroscopy. Most are also supported by u.v. spectroscopy and mass spectrometry.

(*Received*, 8*th February* 1974; *Com.* 175.)

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