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1,3,7,9-TETRAMETHYL-8,9-DIHYDROXANTHINE AND ITS CHEMICAL PROPERTIES

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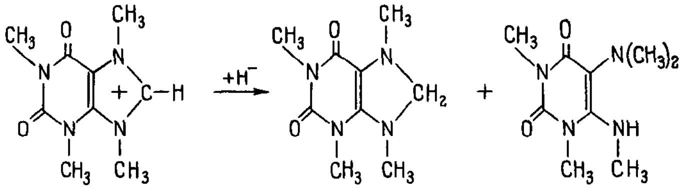
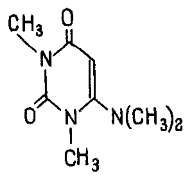
Working on some benzimidazole derivatives we have shown that imidazolium cations, being isoelectronic analogues of the tropilium cation, can add a hydride-ion and be transormed into Δ^4 -imidazolines. The reaction is reversible; the imidazolines -similar to tropilidene-readily give up a hydride-ion to various acceptors, and are changed into the imidazolium ions. Among any isoelectronic analogues of tropilium, the imidazolium ions have been found the least electrophilic, whereas the imidazolines are the most powerful hydride-ion donors (1-3).

We have found that the 1,3,7,9-tetramethylxanthinium cation (I) can be readily reduced in aqueous solution by sodium or potassium borohydrides to yield the 1,3,7,9-tetramethyl-8,9-dihydroxanthine (II).This reaction is accompanied by the destruction of the imidazolium ring and formation of the 1,3-dimethyl-4-methylamino-5-dimethylaminouracil (III) as a by-product. The PMR spectrum of the latter in D_2O reveals a signal of the dimethylamino group (δ2.95 p.p.m.) in the same position as that for the dimethylamino group of the 1,3-dimethyl-5-dimethylaminouracil (IV), whereas the signal for the 4-methylamino group (3.37 p.p.m.) appears within the field of the 4-dimethylamino group (3.20 p.p.m.) of the 1,3-dimethyl-4-dimethylaminouracil (V), (4).



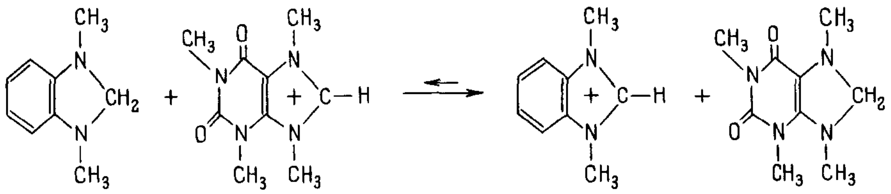
(I) (II) (III)



(V)

Compound (II), like the 1,3-dimethylbenzimidazoline (VI), (1,2) readily gives up a hydride-ion to triphenylchlormethane, triaryltetrazolium cations, carbon tetrachloride, iodine, silver nitrate, and in so doing transforms into the 1,3,7,9-tetramethylxanthinium cation. Its reaction with sulphur and selenium is less smooth than the 1,3-dimethylbenzimidazoline (3), producing 8-thione and 8-selenone in 40-50% yields together with the evolution of CH_3SH and CH_3SeH respectively. The differentiation of the reducing powers of compounds (II) and (VI) was therefore not achieved.

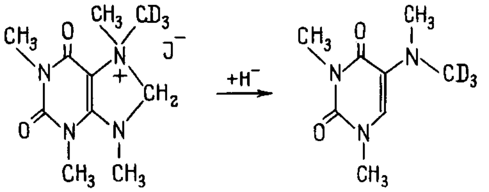
In an acetonitrile solution, the 1,3,7,9-tetramethylxanthinium perchlorate forms a difficultly soluble crystalline complex (VII) with the 1,3-dimethylbenzimidazoline. After heating for 10 hrs. at 100°C the former changes into a crystalline complex (VIII) formed of the 1,3-dimethylbenzimidazolium perchlorate (IX) and compound (II). Both the complexes differ from the original imidazoline derivatives (II, VI) as they are much more stable on keeping in the air, they crystallize from polar solvents (acetonitrile and spirit)and are completely decomposed into their components on boiling in benzene. On heating in acetonitrile only a small fraction of complex (VIII) was changed into complex (VII). Thus, an equilibrium of the hydride-ion distribution between tetramethylxanthinium and the 1,3-dimethylbenzimidazolium cations is strongly in the xanthinium direction, proving that the imidazolium nucleus in tetramethylxanthinium is more electrophilic than that of the benzimidazolium. This fact was also proved by measuring the reduction potentials ($E_{1/2}$ by polarographic methods) of both the tetramethylxanthinium and 1,3-dimethylbenzimidazolium cations, which were found to be - 1.60 and - 1.82 V respectively.



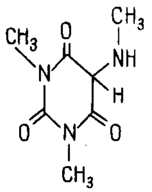
(VI) (I) (IX) (II)

In this case, the hydride-ion is redistributed between the imidazolium ions possessing different electrophilicity, as observed previously (3).Parnes et.al. showed that the tropilium cation can break off a hydride-ion from tropilidene, forming a new carbonium ion of equal electrophilicity with the original cation (5). The possibility of a similar reaction with compounds (VI)and (IX) was investigated by reacting the 1,3-dimethylbenzimidazoline with the 1,3-dimethyl-2-deuterobenzimidazolium perchlorate in CH_3CN and CH_3OD at 20° and 100°C. The perchlorate was obtained by crystallization of compound (IX) from D_2O or CH_3OD. The PMR spectrum of the 1,3-dimethylbenzimidazoline (VI), separated after the reaction, revealed no deuterium in its methylene group (with accuracy ± 2%). Thus the redistribution of the hydride-ion between compounds (VI) and(IX) did not take place. Unlike tropilidene, the 1,3-dimethylbenzimidazoline (VI) is a base; its presence in the reaction mixture helps the polarization of the imidazolium bond: C_2 H and formation of an ylid. Probably the carbon atom of the ylid, carrying a negative charge, cannot be a hydride-ion acceptor, unless the hydride transference leads to the formation of a less electrophilic and more stable carbonium ion.

With electrophilic reagents, the 1,3-dimethylbenzimidazoline undergoes a hydride disproportionation with formation of the 1,3-dimethylbenzimidazolium and accordingly N-substituted-N,N-trimethyl-o-phenylenediamine (3).In analogous conditions compound (II) with CH_3J gives only a methiodide (X), which can be reduced in aqueous solution by KBH_4 to the 1,3-dimethyl-5-dimethylaminouracil (IV). The reaction with CD_3J gives a methiodide whose reduction product (IV) on PMR spectrum shows a signal for the dimethylamino group, which has half the intensity of the unlabelled compound.



(X) (IV)



This shows a quaternisation of the amino group located at position 7 of the compound (II), and the cleavage of the salt formed by breaking of the C_8 - N_7 and C_6 - N_9 linkages. These linkages were also broken when compound (II) was subjected to acidic hydrolysis with the formation of 7-methyluramile.

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