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REACTIVITY AND ELECTRONIC STRUCTURE OF A 4,5-DIDEHYDROPYRIMIDINE

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Abstract: The reaction of 2-t-butyl-4,5-didehydropyrimidine (2) with 1,3-dienes, two 1,3-dipoles (azides), an electrophile (iodine) and a nucleophile (ethanol) has been investigated. The results are correlated with the electronic structure of 4,5-didehydropyrimidine calculated by an ab initio quantum chemical method.

Although 4,5-didehydropyrimidines have been postulated as intermediates in a number of aromatic nucleophilic substitutions carried on halogenopyrimidines, cogent arguments in favour of their existence are scarce (1). The best evidence is still the trapping of 2-t-butyl-4,5-didehydropyrimidine (2), generated by the oxidative method developed by Campbell and Rees (2), with furan (3). Since then, we have investigated the reactivity of this intermediate toward several 1,3-dienes, two 1,3-dipoles, an electrophile and a nucleophile. The results are recorded in this communication and correlated with the ab initio calculated electronic structure of the parent intermediate.

STO-3G (4) calculations of the charge distribution in 4,5-didehydropyrimidine, resting on a recently optimized geometry (5), yielded populations for C4 and C5 of 5.845 and 6.106 electrons (these values qualitatively agree with the results of earlier extended Hückel calculations using unoptimized benzene-type geometries (6)). The important polarization of the triple bond can be visualized as a ynamine-like delocalization of the adjacent nitrogen lone pair into the planar "extra" bond. This is also clearly shown in the STO-3G Molecular Electrostatic Potential (MEP) computed in the molecular plane.

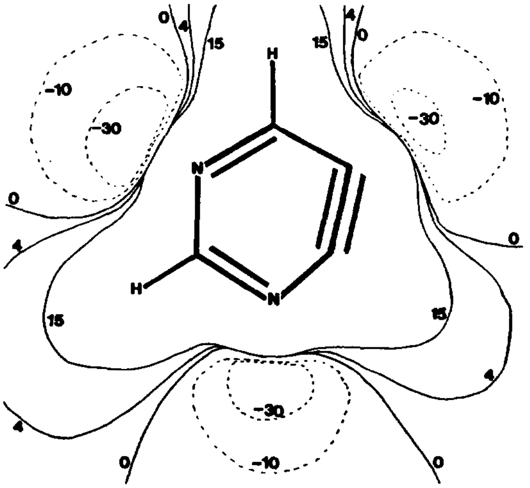
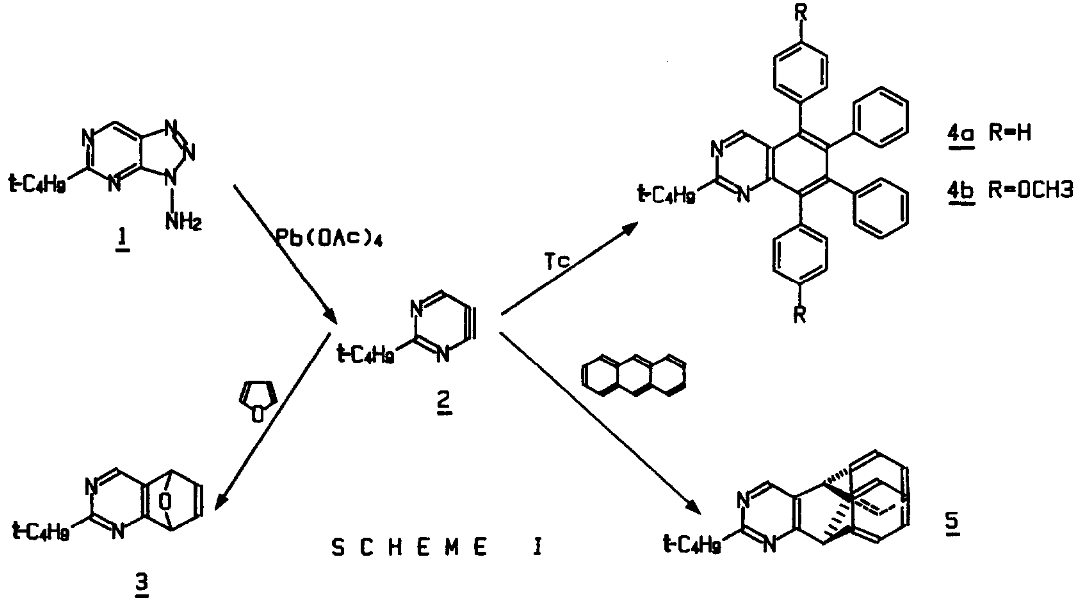


Figure: STO-3G MEP map for 4,5-didehydropyrimidine (molecular plane - contour values in Kcal/mol with 1 Kcal = 4.184 KJ)

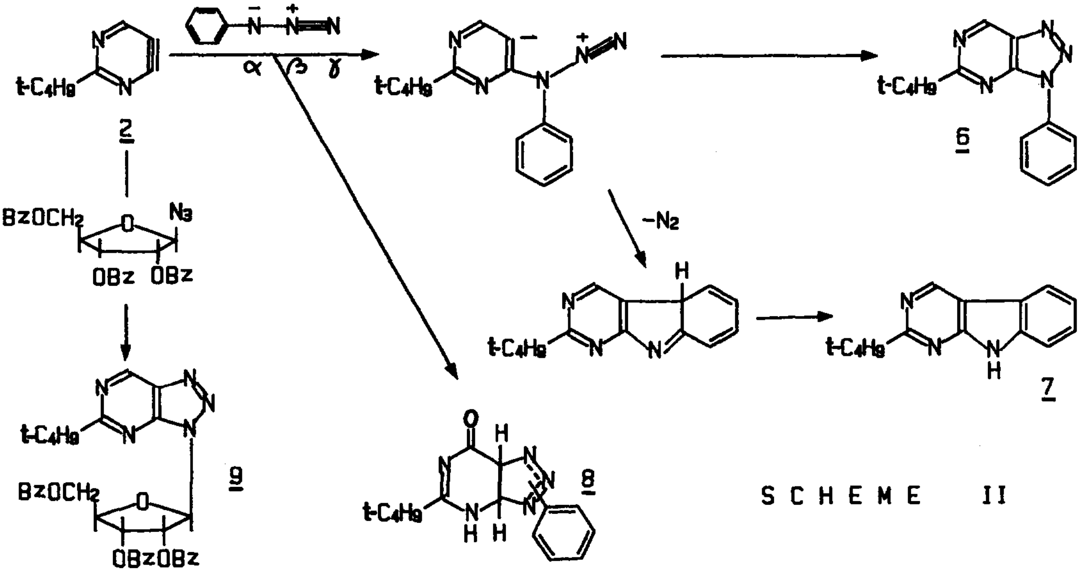
3-Amino-5-t-butyl-3H-v-triazolo(4,5-d)pyrimidine (1), whose synthesis has recently been reinvestigated (7), served as the precursor. Except where otherwise indicated, its oxidation with lead tetra-acetate (1.2 equivalent) was carried out in dichloromethane, at room temperature, in the presence of 3 equivalents of trapping agent. The products were isolated by preparative t.l.c. and identified by P.M.R. spectroscopy and mass spectrometry.

Reaction with 1,3-dienes (scheme I). Cycloaddition of 2-t-butyl-4,5-didehydropyrimidine (2) to furan, 2,3,4,5-tetraphenylcyclopentadienone (tetracyclone, Tc), 2,5-di-(p-methoxyphenyl)-3,4-diphenylcyclopentadienone and anthracene respectively afforded 5,8-epoxy-5,8-dihydro-2-t-butylquinazoline (3) (9%, m.p. 92-94°), 5,6,7,8-tetraphenyl-2-t-butylquinazoline (4a) (27%, m.p. 269-271°, yellow fluorescence at 350 nm), 5,8-di-(p-methoxyphenyl)-6,7-diphenyl-2-t-butylquinazoline (4b) (15%, m.p. 211-213°, white fluorescence) (8) and the 1,3-diazatriptycene 5 (traces). Significantly, the yield of the cycloadduct 3 rose to 50% when furan was used as co-solvent. On the other hand, although the relative reactivities of the above dienes are the same as in the case of similarly generated benzyne (9), the yields are much lower. A possible explanation for this is that the highly polarized triple bond decreases orbital control in favour of charge control.



SCHEME I

Reaction with 1,3-dipoles (scheme II). The intermediate 2 reacted with a large excess of phenyl azide to give a mixture of three products: 3-phenyl-5-t-butyl-3H-v-triazolo(4,5-d)pyrimidine (6) (44%, m.p. 126-127°), 2-t-butyl-9H-pyrimido(4,5-b)indole (7) (19%, m.p. 194-195°) and compound 8 (7%, m.p. 117-121°) whose structure is considered tentative. The identity of products 6 and 7 is supported by an unequivocal synthesis in which the former is converted to the latter by photolysis (8). This conversion however does not account for the presence of the pyrimido-indole 7 in the cycloaddition experiments since the same yields were obtained in the dark. Furthermore, neither acid nor lead di- and tetra-acetate promote the transformation of the triazolo-pyrimidine 6 into compound 7. Its formation, rationalized as shown, would be indicative of a charge controlled process in which C4 - Nα interaction between the hetaryne 2 and the reactant predominates. Indeed, ab initio STO-3G calculations for phenyl azide, using a standard geometry (10) (except for the two N N distances (11)), showed that the atomic electronic populations of Nα, Nβ and Nγ are 7.220, 6.893 and 6.996.

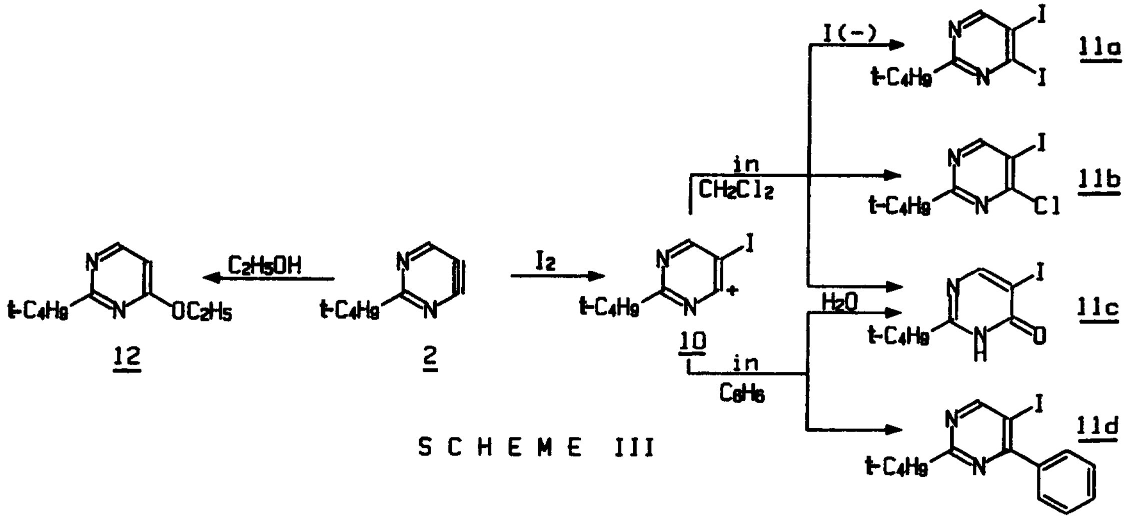


SCHEME II

It was tempting to employ the intermediate 2 as a building-block in nucleoside synthesis. When allowed to react with 2,3,5-tri-O-benzoyl-β-D-ribofuranosyl azide (12), it produced a compound (15%, syrup) to which structure 9 was assigned.

Reactions with an electrophile and a nucleophile (scheme III). Generation of 2-t-butyl-4,5-didehydropyrimidine (2) in the presence of iodine (1.2 equivalent) unexpectedly gave an oily mixture of 4,5-diiodo- and 4-chloro-5-iodo-2-t-butylpyrimidine (11a and 11b) (1.5% and 40% respectively, based on the P.M.R. spectrum) and 5-iodo-2-t-butyl-4(3H)-pyrimidinone (11c) (24%, m.p. 205-206°). Worth to note, boiling sodium hydroxide solution completely hydrolysed the oily mixture to the pyrimidinone 11c. In order to avoid any halogen exchange with halogenated solvents (13), we next used benzene. In this case, a substantial yield of 5-iodo-4-phenyl-2-t-butylpyrimidine (11d) (40%, m.p. 77°) was isolated together with the pyrimidinone 11c (43%); the diiodo-derivative 11a was not detected.

Generation of the hetaryne 2 by oxidation also provided an opportunity to examine its behavior toward uncharged nucleophiles. Thus, experiments were performed in the presence of large amounts of ethanol. The only product obtained was 4-ethoxy-2-t-butylpyrimidine (12) (50%, oil).



SCHEME III

First of all, these results strongly suggest a stepwise mechanism. Secondly, addition of the nucleophile as well as the electrophile seems to be regiospecific, an observation which is easily reconciled with the highly polarized nature of the triple bond. By comparison, much lower dissymetry is found around the triple bond in the MEP of 3-fluorobenzyne for which nucleophilic additions are almost regiospecific (14).

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