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IMIDAZOLES AND PYRAZOLES FROM ISONITROSOFLAVANONES AND SCHIFF BASES

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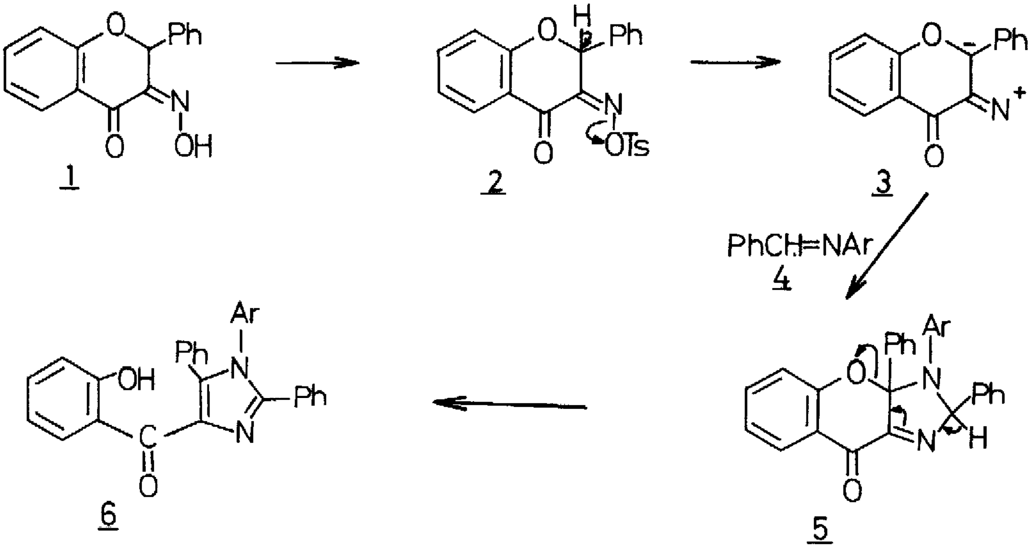
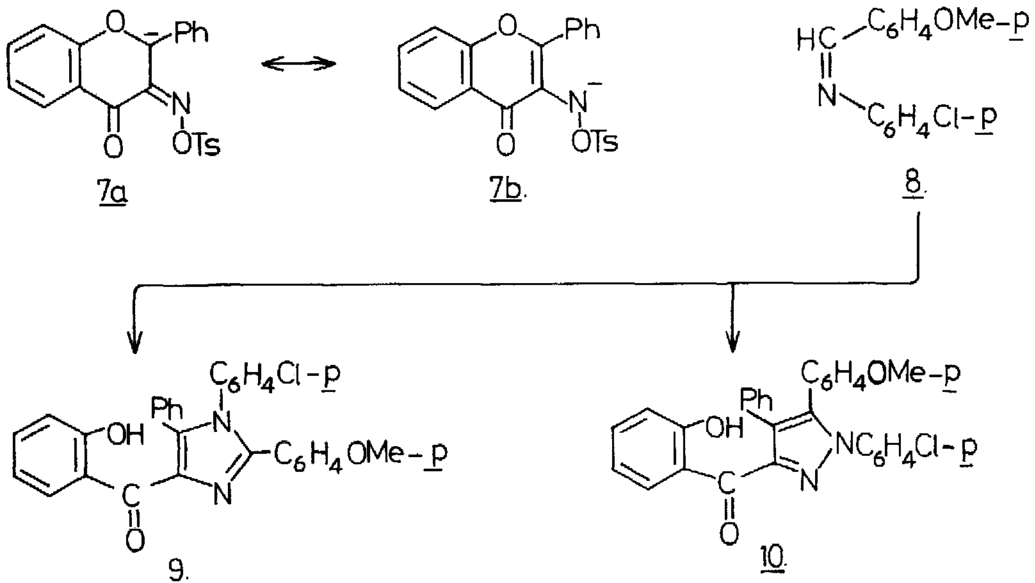
Isonitrosoflavanone tosylate (2) [prepared in situ in CH_2Cl_2 at -30°C from isonitrosoflavanone (1), TsCl and NEt_3] reacts with Schiff bases (4a-d) [refluxed 3 hr in benzene or toluene solvent after removing the CH_2Cl_2] to yield 4-o-hydroxybenzoyl imidazoles (6a-d).[2]



Scheme 1: in 4, 5, and 6 the Ar group is a = Ph; b = p-MeC_6H_4; c = p-ClC_6H_4; d = p-OMe C_6H_4. Details of products: 6a prisms, m.p. 177-179°C; 6b prisms, m.p. 201-203°C; 6c needles, m.p. 241-243°C; 6d needles, m.p. 225-226°C.

We believe that the reaction sequence involves cycloaddition of the 1,3-dipolar species 3 to the Schiff base 4 to form intermediates 5 which undergo deprotonation and ring-opening to give the products 6. Alternatively the ambident anion 7 may add to the C-atom of the Schiff base through the nitrogen atom (cf 7b). For the p-tolyl derivative (6b) the structure was determined by X-ray crystallography.

Crystal structure information for 6b: monoclinic, space group $P2_1/n$, with $Z = 4$. At -40°C, $a = 19.277(4)$, $b = 9.600(2)$, $c = 12.307(2)$ Å, $\beta = 92.31(1)^{\circ}$. A full-matrix least-squares refinement of 386 variables using 2241 reflections (Syntex diffractometer) converged at a conventional R of 0.048 (see Fig 1).


7a 7b. 8.

9.

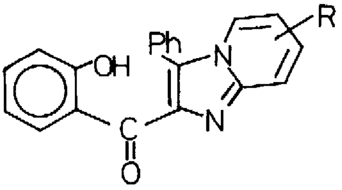
m.p. 212–214°C (yellow needles)

10.

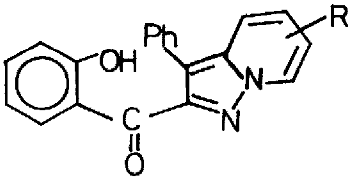
m.p. 204–207°C (prisms)

However, Schiff's base 8 derived from anisaldehyde and p-chloroaniline gave with 2 a mixture of two isomeric cycloadducts to which we assign the structures 9 and 10. All the imidazoles 6a - 6d and 9 showed very similar UV spectra ($\lambda_{max.}$ 260-265 and ca 340 nm) which differ from that of the pyrazole 10 ($\lambda_{max.}$ 246 and 280 nm). The formation of pyrazole 10 could again involve either cycloaddition to dipolar species 3 or reaction of ambident anion 7 through form 7a.

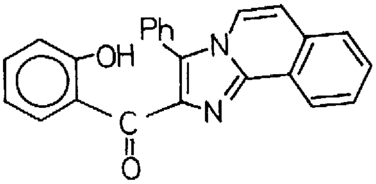
The reactions reported above are an extension of the reaction of isonitrosoflavanone tosylate (2) with pyridine bases, described by one of us.[3] Previously it was not possible to certainly distinguish between structures of types 11 and 12 for these products, although 12 was considered more probable. However, X-ray analysis of the compound from 4-picoline shows it to be the imidazopyridine (11, R = 7-CH_3). Similarly, X-ray analysis of the compound from isoquinoline demonstrates it to be 13; all the other compounds previously described[3] are probably also of structure type 11.



11



12



13

Crystal structure information for 11 (R = 7-CH_3): orthorhombic, space group $P2_12_12_1$, with Z = 4. At -40°C, a = 11.509(2), b = 20.358(2), c = 7.028(1) Å. Refinement: 230 variables, 1612 reflections, R = 0.097; hydrogen atoms were not included as the structure is disordered, particularly with respect to the location of 0(19), the phenolic oxygen atom (cf Fig 2).

Crystal structure information for 13: monoclinic, space group $P2_1/c$, with Z = 8. At -40°C, a = 11.387(4), b = 23.160(9), c = 13.784(4) Å, β = 101.00(3)°. Refinement: 633 variables, 3824 reflections, R = 0.042 (cf Fig 3).

We cannot yet define the structural features which control the relative proportions of products of type 6, 9 and 11 on the one hand or 10 and 12 on the other produced in these reactions, but we are currently working on the elucidation of the details of the reaction mechanism. Previous cycloadditions of azomethines to give imidazole derivatives[4] are of a different type.

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FOOTNOTES AND REFERENCES

(1) Part of this work was carried out while on leave of absence at the University of East Anglia.

(2) Satisfactory analytical data were obtained for all new compounds described.

(3) M. Michalska, Tetrahedron Letters 2667 (1971).

(4) R. Huisgen, V. Martin-Ramos and W. Scheer, Tetrahedron Letters 477 (1971).

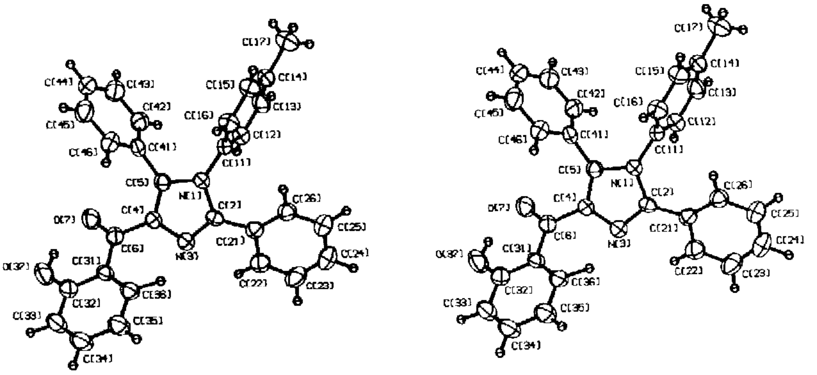

FIGURE 1. X-Ray crystal structure of 4-o-hydroxybenzoyl-2,5-diphenyl-1-p-tolylimidazole (6b).

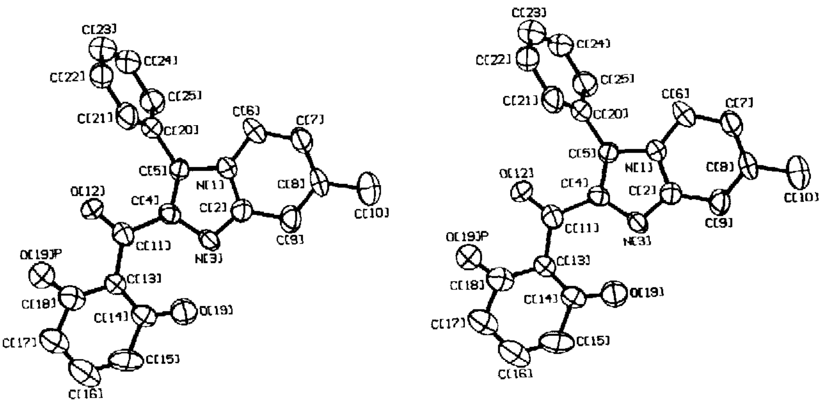

FIGURE 2. X-Ray crystal structure of 2-o-hydroxybenzoyl-7-methyl-3-phenylimidazo [1,2-a]pyridine.

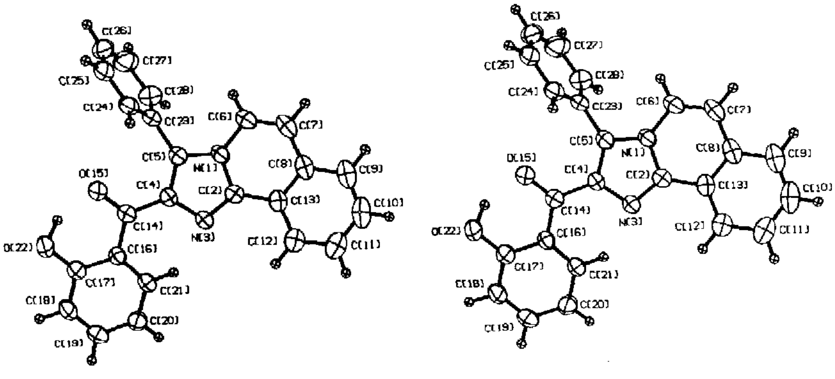

FIGURE 3. X-Ray crystal structure for 2-o-hydroxybenzoyl-3-phenylimidazo[1,2-a] isoquinoline (13).