REACTIONS OF ARYLPROPIOLAMIDES WITH ARYLACETAMIDES

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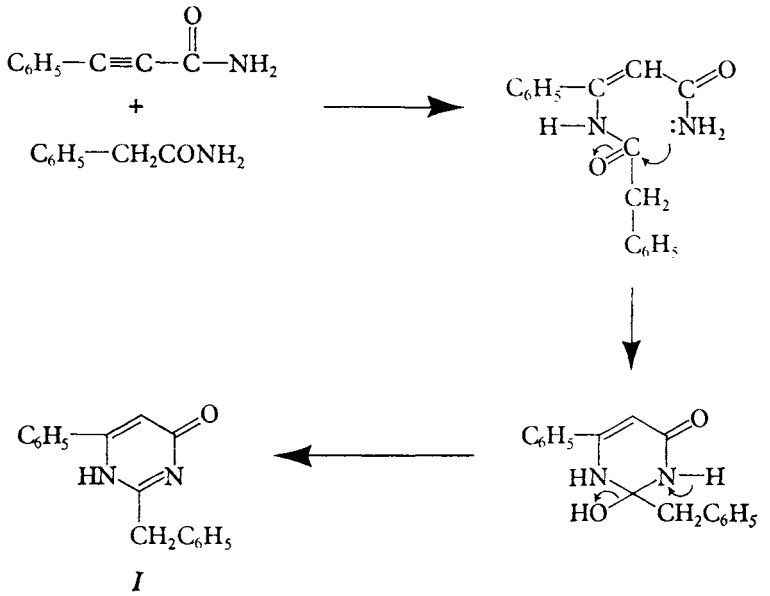
The reaction of 3-phenylpropiolamide with phenylacetamide yielded 2-benzyl-4-phenyl-6-pyrimidone, whilst that of *o*-chlorophenylpropiolamide with phenylacetamide or *p*-chlorophenylacetamide yielded the 4-(*o*-chlorophenyl)pyrimidine-2,6-dione. The reaction products were identified from their spectral analysis.

Moureu and Lazennac[1-4] have described the condensation reactions of acetylenic amides with phenols, primary and secondary amines. The corresponding products were found to be β-aryloxylacrylamide, β-aminoacrylamides, 5-isoxazolones, and 5-pyrazolones, respectively. Worall and his coworkes[5,6] reported the condensation reaction of acetylenic thioamides with hydroxylamine, which yielded the substituted 5-amino-3-phenyl isoxazolone. The reaction products were also found to include 2-phenacylbenzthiazole and 2-penthiazole derivatives in small yields. Worall[7,8] also

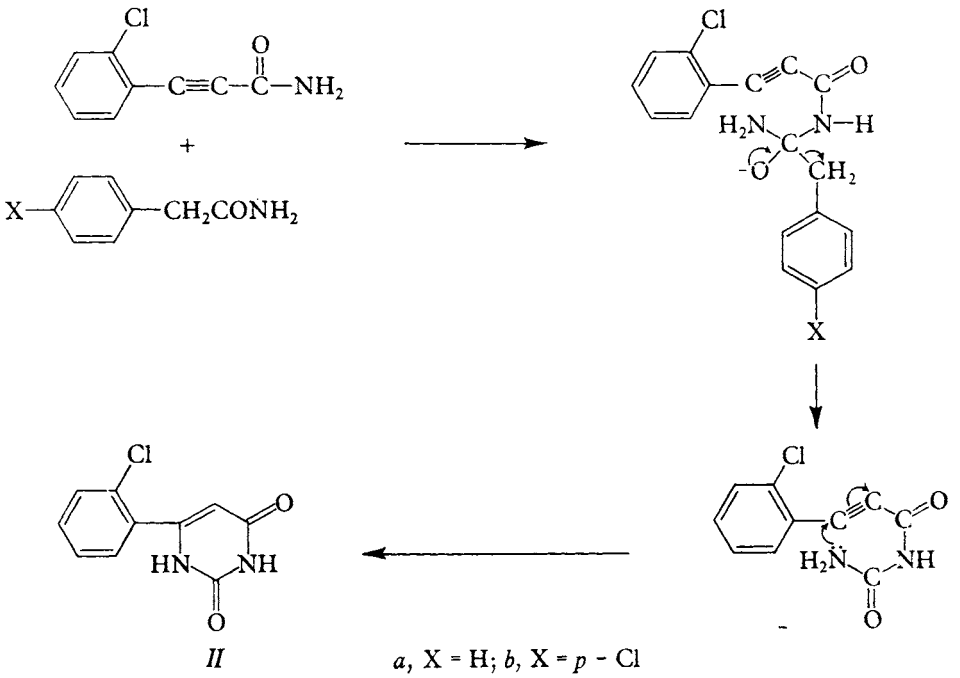


I

SCHEME 1

studied the action of hydrazine and phenylhydrazine on the thioamide of propiolic acid which was found to give substituted 3-phenyl-5-aminopyrazoles. In the present work, the reactions of arylpropiolamides with arylacetamides were carried out in the presence of powdered sodium in boiling benzene. It was found that the reaction of arylacetamides with phenylpropiolamide and with *o*-chlorophenylpropiolamide did not yield analogous products, *i.e.* the reactions proceeds *via* different mechanisms. 2-Benzyl-4-phenyl-6-pyrimidone was obtained as the major product from the reaction between phenylacetamide and phenylpropiolamide. The reaction mechanism suggested a Michael condensation of the anion $PhCH_2\overset{(-)}{C}ONH$ with subsequent cyclisation and elimination of water molecule (Scheme 1).

Whilst an exchange occured between the anion formed from phenylacetamide and propiolamide itself to form the corresponding anion from *o*-chlorophenylpropiolamide followed by attack to the carbonyl group of the phenylacetamide (Scheme 2). This may be because that Michael addition of the anion $ArCH_2\overset{(-)}{C}ONH$ to the triple bond of the acetylenic amide doesn't take place due to steric effect caused by chlorine in the *ortho* position.



II *a*, X = H; *b*, X = *p* - Cl

SCHEME 2

The infrared and proton magnetic resonance spectral data for compound *I* are consistent with the proposed structure. The infrared spectral data shows an absorption band at 1 600 cm^{-1} for the aromatic system. An absorption band at 1 615 cm^{-1} was attributed to the presence of >C=N— group of the pyrimidine ring[9]. A sharp band at 1 660 cm^{-1} confirmed the presence of a carbonyl group, and another broad band at 3 250 cm^{-1} was attributed to —NH stretching frequency. The proton magnetic resonance spectral data showed a multiplet at δ 7·45–8·04 (10 H), due to the aromatic protons. A singlet at δ 3·92 (2 H), indicated an arylmethylanic group, deshielded by the >C=N— function. The —NH protons was observed as a broad singlet at δ 12·63 (exchangable with deuterium oxide). The infrared and proton magnetic resonance spectral data for compound *II* are consistent with the suggested structure. The infrared spectral data, showed a three-band system at 1 660, 1 720, and 1 770 cm^{-1} in agreement with the presence of an unsaturated cyclic imide system[10–12]. The NH stretching bands appeared at 3 200 and 3 400 cm^{-1}. The proton magnetic resonance spectral data showed a multiplet at δ 7·30–8·15 (4 H), due to aromatic protons. A singlet at δ 6·77 (1 H),was due to the olefinic protons. The imido protons showed a resonance signal at δ 12·63 (2 H), these were found to be exchangable with deterium oxide. The ultraviolet absorption spectra also supported the suggested structure, since a red shift from λ_{max} 314 nm to 325 nm was obtained when the spectrum was run under alkaline conditions.

EXPERIMENTAL

IR spectra were measured in chloroform using a Unicam SP 200 instrument. ^1H NMR spectra were determined with a Varian A-60D spectrometer for solutions in C^2HCl_3 and deutrated dimethyl sulfoxide containing tetramethylsilane as internal standard. UV spectra were measured in ethanol with a Unicam SP 800 instrument. Compounds were analysed by Alfred Bernhardt, Max Planck Institute, Ruhr, F.R.G. Melting points were determined on a Kofler hot stage and are uncorrected.

Condensation of Phenylacetamide and Phenylpropiolamide

Phenylacetamide (1·18 g) and powdered sodium (0·2 g) in benzene (150 ml) was kept under reflux for 22 h; then phenylpropiolamide (1·27 g) was added and the heating under reflux continued for another 3 days. Water (200 ml) was added to the mixture and the benzene layer was separated, dried over sodium sulphate and evaporated to give the unchanged phenylacetamide. The alkaline aqueous layer was acidified with dilute sulphuric acid and extracted with ether. The ethereal solution was shaken with an aqueous solution of sodium hydrogen carbonate, dried and evaporated to give a brown solid, which was recrystallized from benzene to give 2-benzyl-4-phenyl--6-pyrimidone (*I*) as yellow plates, m.p. 218–219°C. UV spectrum λ_{max} (ethanol): 242, 286 nm; log ε 4·20, 3·91. IR spectrum, $\nu(CHCl_3)$: 1 600 (aromatic), 1 615 (C=N), 1 660 (C=O), 3 250 (NH) cm^{-1}. NMR spectrum $\delta(C^2HCl_3)$: 7·43–8·10 (m, ArH), 3·92 (s, Ar–CH_2), 12·60 (broad, exchangable, NH). For: $C_{16}H_{14}N_2O$ (218·2) calculated: 77·8% C, 5·3% H, 10·6% N; found: 77·9% C, 5·4% H, 10·3% N.

Condensation of Phenylacetamide and *o*-Chlorophenylpropiolamide

Phenylacetamide (1·18 g) and powdered sodium (0·2 g) in benzene (150 ml) was kept under reflux for 22 h; then *o*-chlorophenylpropiolamide (1·6 g) was added and the heating under reflux continued for another 6 h. The mixture was treated as described above. The alkaline aqueous layer after acidification and extraction with ether yielded solid recrystallises from benzene to give yellow crystals (1·1 g) of 4-(*o*-chlorophenyl)-pyrimidine-2,6-dione (*II*) m.p. 260–261°C. UV spectrum λ_{max} (ethanol): 221, 314 nm; log ε 3·41, 3·57. ν($CHCl_3$): 1 770, 1 720, 1 660 (two C=O and C=C of the cyclic imide system), 3 200–3 400 (two NH) cm^{-1}. δ($C^2H_3SOC^2H_3$): 7·33 to 8·05 (m, ArH), 5·74 (broad, exchangeable, NH), 6·32 (s, C=CH). For $C_{10}H_7ClN_2O_2$ (222·5) calculated: 53·9% C, 3·1% H, 12·6% N, 15·9% Cl; found: 54·1% C, 3·4% H, 12·2% N, 15·5% Cl.

Condensation of *p*-Chlorophenylacetamide and *o*-Chlorophenylpropiolamide

p-Chlorophenylacetamide (1·48 g) and powdered sodium (0·2 g) in benzene (150 ml) was kept under reflux for 24 h; then *o*-chlorophenylpropiolamide (1·6 g) was added and the heating under reflux continued for another 72 h. The mixture was treated as described above. The alkaline aqueous layer after acidification and extraction with ether yielded solid which recrysallise from benzene to give 1·3 g of 4-(*o*-chlorophenyl)-pyrimidine-2,6-dione (*II*) m.p. 259–260°C. The mixed melting point with compound obtained in the previous experiment was undepressed.

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