Chemistry of Heterocyclic Compounds, Vol. 39, No. 6, 2003

REACTION OF 1,2-DIAMINO-4,5-DIPHENYLIMIDAZOLE WITH 1,3-DIARYLPROPENONES AND THEIR DIBROMO DERIVATIVES

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The reaction of 1,2-diamino-4,5-diphenylimidazole with 1,3-diarylpropenones and 1,3-diaryl-2,3-dibromopropenones gives dihydro- and heteroaromatic derivatives of 6-hydroxyimidazopyrimidines and also imidazopyrimidines which do not contain the 6-hydroxy group. It was found that the structure of the products depended on the conditions for carrying it the reaction.

Keywords: diaminoimidazole, 1,3-diarylpropen-1-one, ^{1}H NMR spectra, stereoselectivity.

In a continuation of the investigated reactivity of vicinal diaminoazoles which contain an N-amino group [1-4] we have studied the reaction of 1,2-diamino-4,5-diphenylimidazole (**1**) with the chalcones **2a-d** and the 1,3-diaryl-2,3-dibromopropanones **3a-c**. The substitution of a hydrogen atom by a phenyl ring at the most nucleophilic reaction center of the diamine molecule **1** (the carbon atom at position 5 of the imidazole ring) can lead to a change in the reaction course when compared with similar reactions of 1,2-diamino-4-phenylimidazole (in which imidazopyridazine systems are formed [1, 3]). This is also indicated in studies [5] in which the reaction of diamine **1** with the chalcone **2a** gives polyphenyl-substituted derivatives of imidazopyrimidines, its dimer, and 5-hydroxydihydroimidazopyrimidine. However, the formation of the 5-hydroxy derivative contradicts the evidence obtained previously [6] regard this type of cyclocondensation reaction and needs verification.

The reaction of the diamine **1** with the chalcones **2a-d** can be brought about by refluxing them in DMF for 3 h. In this way the compounds **4a-d** (see Table 1) were separated from the reaction mixture in 20-30% yields. Additionally, during the course of the reaction, a mixture of hard to identify, oily products are formed together with up to 30% of unreacted starting diamine and this explains the low yields of the products **4a-d**.

The IR spectra of compounds **4a-d**, recorded as KBr tablets, show the absence of bands in the region 3200-3300 cm^{-1} whereas the spectra of CCl_4 solutions show a narrow peak in the region 3560 cm^{-1}. The electronic absorption spectra of compounds **4a-d** are quite uniform and are characterized by bands in the region of 270 and 386 nm and are rather insensitive to the electronic nature of the substituents R and R'.

The ^{1}H NMR spectra of the products **4a-d** show a multiplet for the protons of the four aromatic substituents in the region 7.00-8.50 ppm together with three similar singlets at 5.00-7.00 ppm which are: a broad or weakly split singlet with a chemical shift of 5.00, a singlet at 5.30, and a lowfield singlet at 6.60-6.90 ppm which disappears under conditions of deuterium exchange. Hence the ^{1}H NMR and IR spectroscopic data lend support to the presence of the OH group in the molecules of compounds **4a-d**.

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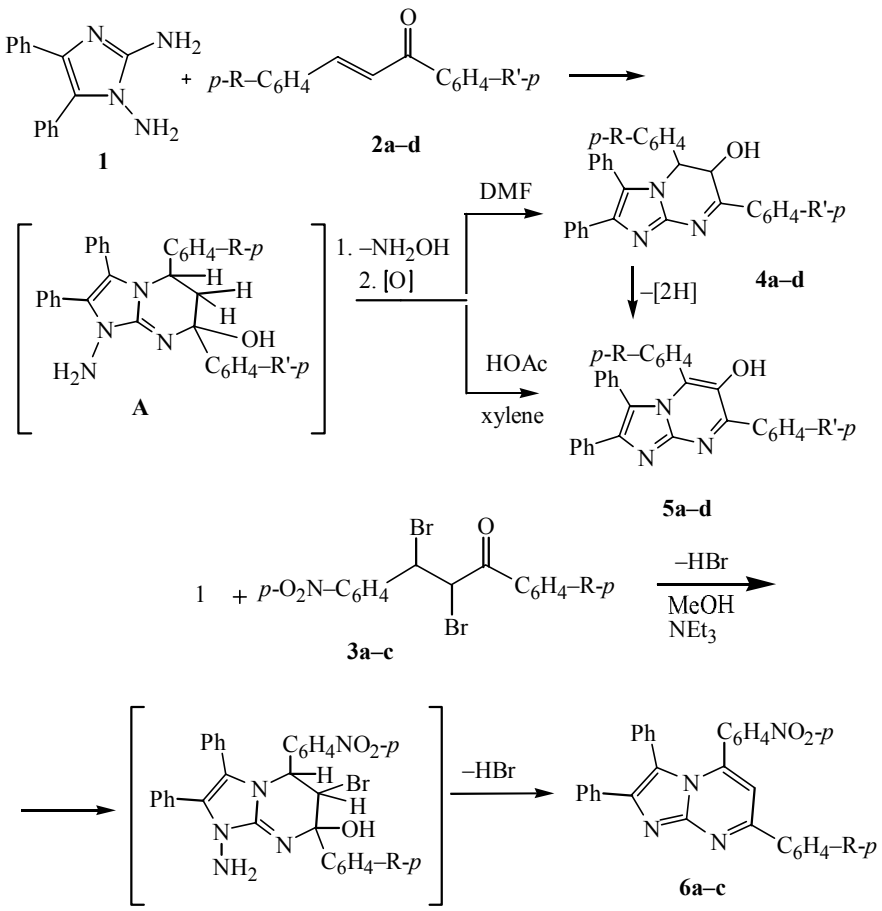
TABLE 1. Characteristics for the Compounds Synthesized

Compound	Empirical formula	Found N, % / Calculated N, %	mp, °C	IR spectrum, ν, cm^{-1}: C=S, C=N (in KBr)	IR spectrum, ν, cm^{-1}: OH (in CCl_4)	UV spectrum, λ, nm (ε×10^{-3})	^{1}H NMR spectrum, δ, ppm (*J*, Hz)	Yield, %
4a	$C_{30}H_{23}N_3O$	9.4 / 9.5	240-241	1650	3564	270 (18.2), 384 (15.2)	5.00 (1H, s, 5-H); 5.30 (1H, s, 6-H); 6.33 (1H, s, OH); 6.70-8.22 (20H, m, H arom.)	30
4b	$C_{30}H_{22}BrN_3O$	8.0 / 8.1	218-220	1645	3564	272 (19.8), 383 (15.7)	5.00 (1H, s, 5-H); 5.32 (1H, s, 6-H); 6.43 (1H, s, OH); 6.83-8.15 (19H, m, H arom.)	25
4c	$C_{30}H_{22}BrN_3O$	8.0 / 8.1	228-229	1655	3560	270 (19.6), 384 (15.2)	5.05 (1H, s, 5-H); 5.45 (1H, s, 6-H); 6.69 (1H, s, OH); 7.00-8.83 (19H, m, H arom.)	25
4d	$C_{30}H_{22}N_4O_3$	11.4 / 11.5	220-221	1650	3564	272 (19.7), 384 (15.3)	5.09 (1H, s, 5-H); 5.45 (1H, s, 6-H); 6.90 (1H, s, OH); 7.10-8.25 (19H, m, H arom.)	20
5a	$C_{30}H_{21}N_3O$	9.5 / 9.6	230-232	1605	3560	—	7.10-8.20 (20H, m, H arom.) 13.0 (1H, s, OH)	45
5d	$C_{30}H_{20}N_4O_3$	11.5 / 11.6	255-256	1608	3562	—	2.47 (3H, s, CH_3); 7.40-8.40 (16H, m, H arom.); 13.6 (1H, s, OH)	40
6a	$C_{30}H_{20}N_4O_2$	11.9 / 12.0	>300	1626	—	251 (22.7), 390 (8.44)	7.00-7.55 (16H, m, H arom.); 7.85 (2H, d, *J* = 8, H arom.); 8.35 (2H, d, *J* = 8, H arom.)	32
6b	$C_{30}H_{19}BrN_4O_2$	10.1 / 10.2	>300	1622	—	251 (22.7), 392 (10.0)	7.00-7.60 (15H, m, H arom.); 7.88 (2H, d, H arom.); 8.30 (2H, d, *J* = 8, H arom.)	24
6c	$C_{31}H_{22}N_4O_3$	11.1 / 11.2	>300	1620	—	252 (26.0), 393 (10.3)	3.89 (3H, s, CH_3); 7.00-7.50 (18H, m, H arom.); 7.85 (2H, d, *J* = 8, H arom.); 8.30 (2H, d, *J* = 8, H arom.)	20



2, **4**, **5** **a** R = R' = H; **2**, **4** **b** R = Br, R' = H, **c** R = H, R' = Br; **2**, **4**, **5** **d** R = NO_2, R' = H;
3, **6** **a** R = H; **b** R = Br, **c** R = OMe

The use of the INDOR effect in the ^{1}H NMR spectrum of compound **4a** confirms the presence of the CH–CH(OH) fragment in the molecule and its actual existence as a 6-hydroxy dihydroimidazopyrimidine and not a 5-hydroxy structure as had been proposed in the report [5].

The mass spectrum of compound **4c** also supports the formation of a hydroxy derivative and shows the quasimolecular ions [M+H] 519 and 521 whose isotopic composition corresponds to a molecule with a bromine atom present.

The presence of two chiral centers in the molecules **4a-d** infers the potential formation of two diastereomers which should be revealed in their ^{1}H NMR spectra by doubling of the typical signals. This is not observed and so only one of the possible diastereomers is formed in the studied reaction . The absence of a spin-spin interaction between the protons in positions 5 and 6 of the imidazopyrimidine bicycle infers that the H–$C_{(6)}$–$C_{(7)}$–H torsional angle is close to 90°. From the data given in the work [6] such an angle is realized for the vicinal protons of dihydropyrimidine rings with diaxial substituents in positions 5 and 6. In such a ring the 6-hydroxy group and the proton at position 5 are *cis*-oriented and this explains [7] the intertness of such molecules to aromatization *via* dehydration.

Hence the obtained spectroscopic data and also the results of the elemental analysis for nitrogen in compounds **4a-d** (Table 1) agree with the structure of the 5,7-diaryl-6-hydroxy-2,3-diphenyl-5,6-dihydroimidazo[1,2-*a*]pyrimidines. Their formation can be considered as a process occurring *via* a stage of β-hetarylation of the chalcones **2a-d** by the diamine **1** and cyclization to the intermediate **A** with subsequent elimination of the N-amino group. There then occurs an oxidation of the dihydropyrimidine system by the oxygen of the air at the $C_{(6)}$–H bond of the bicycle.

An increase in the time of refluxing the reaction mixture of the diamine **1** with the chalcone **2a** from 3 to 8 h permits the separation of the product of a more exhaustive oxidation which is the 6-hydroxy-2,3,5,7-tetraphenylimidazopyrimidine (**5a**).

Compounds **5a,d** were separated as the basic products of the reaction under reflux of the diamine **1** with the chalcones **2a,d** in the system xylene–acetic acid. The presence of the hydroxy group is confirmed by the band at 3565 cm^{-1} in the IR spectra of solutions in CCl_4 and also by the lowfield singlet at 13.0 ppm (which disappears under conditions of deuterium exchange) in their ^1H NMR spectra.

Hence, amongst the products of the reaction of the diamine **1** with the chalcones **2**, we have not found one of the compounds reported in the work [5], but the results we obtained are in good agreement with the general ideas concerning the reaction of unsaturated carbonyl compounds with 1,3-binucleophiles [8].

The imidazopyrimidines **6a-c**, not containing a hydroxy group, could be prepared by the prolonged refluxing of the diamine **1** with the dibromo ketones **3a-c** (which contained a nitrophenyl substituent) in ethanol in the presence of triethylamine (Table 1). The first stage in this process is a dehydrobromination with the α-bromochalcone being formed taking part in the β-hetarylation. Fission of the amino group and the subsequent oxidation probably precedes elimination of the second molecule of HBr, hence the formation of hydroxy derivatives is not observed. The structure of the 5,7-diaryl-2,3-imidazo[1,2-*a*]pyrimidines **6a-c** was confirmed by spectroscopic methods (Table 1).

The position of the aromatic proton signals of the 5-nitrophenyl substituent in compounds **6a-c** shows that the same reaction course is preserved in the formation of the heteroaromatic derivatives **6a-c** *via* the reaction of the diamine **1** with the ketones **3a-c**. It is known that an aryl substituent at position 7 of an imidazopyrimidine ring is shifted out of the plane of the bicycle and is observed in the ^1H NMR spectra as a strong, weakly split signal [9]. Indeed, the spectra of the compounds **6a-c** clearly show two doublets which are typical of the protons of a nitrophenyl residue.

EXPERIMENTAL

Electronic absorption spectra for the compounds obtained were measured in ethanol on a Specord M-40 spectrophotometer for a material concentration of 2-5 × 10^{-5} mol/l. IR spectra were taken on a Specord IR-75 spectrometer, and ^1H NMR spectra on a Bruker AM-300 (300 MHz) spectrometer for TMS standard and DMSO-d_6 solvent. Mass spectra were obtained on an MSBK mass spectrometer (Electron Industrial Association, Perm city). Compound ionization was carried out using ^{252}Cf fission fragment bombardment. The ionization energies of the particles were 90-110 MeV, tube length 45 cm, accelerating intensity 20 kV. Spectroscopic accumulation time 15-20 min.

The purity of the compounds was monitored using TLC on Silufol UV-254 plates with ethyl acetate eluent.

6-Hydroxy-2,3,5,7-tetraphenyl-5,6-dihydroimidazo[1,2-*a*]pyrimidine (4a). A solution of the diamine **1** (0.5 g, 2 mmol) and the chalcone **2a** (0.45 g, 2 mmol) in DMF (1 ml) was refluxed for 1 h. After cooling, acetone (15 ml) was added to the reaction mixture and the product **4a** (0.3 g, 30%) was filtered off.

Compounds 4b-d were obtained by a similar method.

6-Hydroxy-2,3,5,7-tetraphenylimidazo[1,2-*a*]pyrimidine (5a). A solution of the diamine **1** (0.5 g, 2 mmol) and the chalcone **2a** (0.45 g, 2 mmol) in xylene (20 ml) and glacial acetic acid (6 ml) was refluxed for 6 h. Solvent was evaporated off in vacuo by two thirds and the compound **5a** (0.3 g, 45%) was filtered off after cooling.

Compound 5d was obtained by a similar method.

5-(4-Nitrophenyl)-2,3,7-triphenylimidazo[1,2-*a*]pyrimidine (6a) A solution of the diamine **1** (0.5 g, 2 mmol) and the ketone **3a** (0.75 g, 2 mmol) in ethanol (25 ml) and methyl morpholine (0.3 ml) was refluxed for 10 h. After cooling, the product **6a** (0.3 g, 32%) was filtered off.

Compounds 6b,c were obtained by a similar method.

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