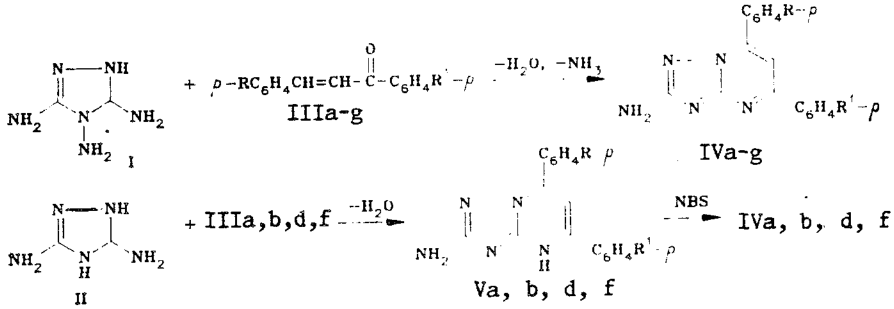
CYCLOCONDENSATION OF CHALCONES WITH DI- AND TRIAMINO-1,2,4-TRIAZOLES

S. M. Desenko, N. N. Kolos, M. Tuéni, and V. D. Orlov

UDC 547.859.1'792.1'538.1:543.422

We have carried out the synthesis of 2-amino-5,7-diaryl-1,2,4-triazolo[1,5-a]pyrimidines from chalcones and 3,4,5-triamino-1,2,4-triazole and synthesized them independently via the 4,7-dihydro derivatives. The course and mechanism of the cyclocondensation are discussed.

In continuation of our studies of the cyclocondensation of aromatic α,β-unsaturated ketones with nitrogen binucleophiles, we have investigated the reaction of 3,4,5-triamino- (I) and 3,5-diamino-1,2,4-triazole (II) with chalcones. Refluxing solutions of the triamine I and ketones IIIa-g in alcohol in the presence of triethylamine or HCl (the conditions for treating o-diamines with unsaturated ketones [1, 2]) were not successful. The reaction was carried out by treating I with chalcones IIIa-g in refluxing DMF. In addition to the formation of the products IVa-g a marked tarring of the reaction mixture was noted, and this had a significant effect on the overall yields (Table 1).



III—V a-e R=H, f R=CH_3O, g R=NO_2; a,f,g R^1=H, b R^1=CH_3, c R^1=CH_3O, d R^1=Cl, e R^1=NO_2

The results of elemental and spectroscopic analysis of the synthesized materials allowed us to exclude dihydro-1,2,4-triazolo[1,5-b]-1,2,4-triazepine structures. The nitrogen content and mass spectrum of IVa (molecular ion m/z 287) unambiguously points to the elimination of not only water but also ammonia. Compound IVa is identical to the previously described 2-amino-5,7-diphenyl-1,2,4-triazolo[1,5-*a*]pyrimidine [3]. This fact, and the similarities in the basic spectral properties for all of the IV series (Table 1), means that IVb-g are 2-amino-5,7-diaryl-1,2,4-triazolo[1,5-*a*]pyrimidines.

To determine the position of the p-R–C_6H_4 and p-R^1–C_6H_4 substituents (for R ≠ R') we have carried out another synthesis of IVa, b, d, f. Cyclocondensation of 3,5-diamino-1,2,4-triazole (II) with ketones IIIa, b, d, f in DMF gave dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines Va, b, d, f, subsequent treatment of which (in alcoholic suspension) with N-bromosuccinimide causes their heteroaromatization to the desired IV. It should also be mentioned that traces (1-5%) of IV are also observed in the course of the condensation itself; most noticeably in the reaction of diamine II with 4'-methylchalcone (IIIb).

The scheme shows the positions of the aryl radicals p-R–C_6H_4 and p-R^1–C_6H_4 in the pyrimidine ring of Vb, d, f in agreement with the formation of this ring via reaction of the endocyclic nitrogen atom with the β-carbon atom of the ketone and condensation of the keto and amino groups [4]. Compound IV, obtained by aromatization of Vb, d, f and condensation of ketones IIIb, d, f with triamine I are identical by IR and TLC analysis.

It is known [5] that aminoazoles can eliminate their "hydrazino" amino group, this process being facilitated by the presence of carbonyl compounds. However, refluxing a solution of I in DMF both with and without addition of benzaldehyde did not give II. In addition, TLC shows that reaction of amine I with ketones IIIb, d, f does not give the dihydro derivatives V,

---

A. M. Gor'kii State University, Khar'kov 310077. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 938-941, July, 1990. Original article submitted December 26, 1988; revision submitted July 12, 1989.

0009-3122/90/2607-0782$12.50

TABLE 1. Synthesized Compounds

Compound	Empirical formula	mp, °C	IR spectrum, cm^{-1}		UV spectrum, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)	Yield, %*
			ν_{NH_2}	$\nu_{C=N}$		
IVa	$C_{17}H_{13}N_5$	198	3296, 3436	1630	261 (16,9), 356 (11,7)	50 (90)
IVb	$C_{18}H_{15}N_5$	220...222	3310, 3390	1635	287 (19,4), 361 (6,4)	45 (50)
IVc	$C_{18}H_{15}N_5O$	202...204	3315, 3490	1635	262 (10,9), 359 (10,2)	35
IVd	$C_{17}H_{22}ClN_5$	210...211	3313, 3460	1632	275 (12,2), 360 (10,1)	45
IVe	$C_{17}H_{12}N_6O_2$	293...295	3296, 3436	1632	282 (22,7), 375 (15,4)	55
IVf	$C_{18}H_{16}N_5O$	200...201	3326, 3386	1633	281 (15,8), 351 (8,7)	42 (71)
IVg	$C_{17}H_{12}N_6O_2$	269...271	3298, 3392	1638	287 (10,6), 370 (8,2)	45
Va	$C_{17}H_{15}N_5$	244	3394, 3481, 3285**	1618, 1669***	292 (3,1)	72
Vb	$C_{18}H_{17}N_5$	193...195	3395, 3485, 3301**	1619, 1664***	289 (4,0)	50
Vd	$C_{17}H_{14}ClN_5$	178...180	3381, 3473, 3341**	1632, 1662***	290 (4,2)	68
Vf	$C_{18}H_{17}N_5O$	251	3393, 3490, 3320**	1624, 1670***	289 (4,7)	65

---

*Yield by method **B** in brackets.

**Value for ν_{NH}.

***Value for $\nu_{C=C}$.

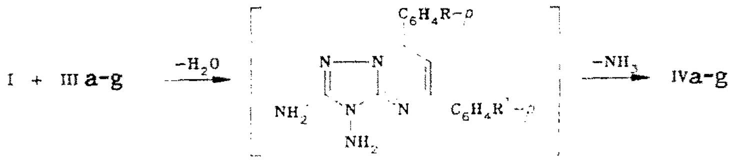
TABLE 2. PMR Spectra of Va, b, d, f in CF_3COOH

Compound	Chemical shift, δ, ppm			
	6-H, d*	7-H, d	aryl protons, m	substituent protons, s
Va	4,97	5,60	6,60...7,50	—
Vb	5,05	5,58	6,55...7,50	1,87 (CH_3)
Vd	5,00	5,60	6,55...7,40	—
Vf	4,97	5,57	6,60...7,30	3,55 (OCH_3)

---

*Spin-spin coupling constant 2.5-3.0 Hz.

even in trace amounts. These results show that separation of an amino group cannot be the first stage of the reaction of triamine I with chalcones. From the data obtained we propose formation of intermediate **A** as a general mechanism for the reaction of chalcones with aminoazoles [4, 6].



A

The analogies in the reactions of amines I and II with chalcones also infer their related pathways. However, heteroaromatization of intermediate A is related only to separation of ammonia and does not demand oxidative reagents. This facilitates the reaction and accounts for the absence of dihydrotriazolo[1,5-*a*]pyrimidines in the reaction products.

The IR spectra of Va, b, d, f show that they exist in the enamine 4,7-dihydro form in the solid state ($\nu_{C=C}$, ν_{NH}, Table 1). The imine and enamine tautomers of dihydroazolopyrimidines are notably different in their electronic spectra [7]. Comparison of the absorption spectra of 5,7-diaryl-4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidines [4] with the spectra of Va, b, d, f (Table 1) shows that introduction of the amino group into position 2 of the bicycle causes an insignificant bathochromic shift (3-5 nm) of the long-wavelength absorption. Hence the 4,7-dihydro structure is retained in Va, b, d, f. The PMR spectra of Va, b, d, f in CF_3COOH solvent (Table 2) show, in addition to a multiplet for the aromatic protons, two doublets for the protons of a CH–CH fragment. This also unambiguously shows the existence of these compounds in the 4,7-dihydro form (probably protonated).

EXPERIMENTAL

IR spectra were measured on a Specord IR-75 instrument in KBr tablets and electronic spectra on a Specord UV-vis in ethanol solvent at a concentration of $(2\text{-}4)\cdot10^{-5}$ molar. PMR spectra were taken on a Tesla BS-487B (80 MHz) instrument using CF_3COOH solvent and TMS internal standard. Mass spectra were recorded for IVa on a Varian MAT-212 (ionization energy 70 eV). The reaction course and product purity were monitored by TLC on Silufol plates eluting with acetone and chloroform.

Elemental analysis for N in the prepared compound agreed with that calculated.

2-Amino-5,7-diphenyl-1,2,4-triazolo[1,5-*a*]pyrimidine (IVa). A. A solution of 3,4,5-triamino-1,2,4-triazole (0.57 g, 5 mmoles) and chalcone (1.04 g, 5 mmoles) in DMF (3 ml) was refluxed for 3 h, cooled, and mixed with benzene (15 ml). The separated oily product was chromatographed on an Al_2O_3 column (activity grade III, 1 cm diameter, filling height 10 cm, eluent chloroform) and the luminescing fraction with R_f 0.25 collected (0.75 g, 50%). Compound IVa had mp 198°C (according to [3], mp 198-200°C). Mass spectrum, m/z (intensity %): 287 (100), 286 (50), 284 (32), 272 (10), 271 (25), 270 (10), 211 (15), 210 (17), 209 (10), 195 (21), 194 (37), 193 (15), 184 (35), 169 (12), 168 (19), 103 (90), 91 (51), 77 (59).

Compounds IVb-g were prepared similarly.

B. N-Bromosuccinimide (0.8 g, 4.5 mmoles) was added in 0.1 g portions to a suspension of 2-amino-5,7-diphenyl-4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidine (Va, 1 g, 3.4 mmoles) in methanol (30 ml) which had been heated to 50-60°C. The reaction mixture was refluxed for 1 h, mixed with KOH (5%, 20 ml), and filtered to give IVa (0.9 g, 90%) with mp 198°C (benzene–DMF, 1:1).

Compounds IVb, d, f were obtained similarly.

2-Amino-5,7-diphenyl-4,7-dihydro-1,2,4-triazolo[1,5-*a*]pyrimidine (Va). A solution of 3,5-diamino-1,2,4-triazole (0.5 g, 5 mmoles) and chalcone (1 g, 4.8 mmoles) in DMF (1 ml) was refluxed for 15 min, the precipitate filtered hot, and washed with methanol and acetone to give Va (1 g, 72%) with mp 244°C (benzene–DMF, 1:1).

Compounds Vb, d, f were obtained similarly.

LITERATURE CITED

1. V. D. Orlov, N. N. Kolos, F. G. Yaremenko, and V. F. Lavrushin, *Khim. Geterotsikl. Soedin.*, No. 5, 697 (1980).
2. I. Z. Papiashvili, "Reaction of heterocyclic ortho-diamines with ketones," Dissertation, Candidate of Chemical Science, Khar'kov (1983).
3. V. A. Chuiguk and T. I. Glukhova, *Ukr. Khim. Zh.*, **46**, 835 (1980).
4. V. D. Orlov, S. M. Desenko, K. A. Potekhin, and Yu. T. Struchkov, *Khim. Geterotsikl. Soedin.*, No. 2, 229 (1988).
5. G. A. Kuz'menko, V. V. Kuz'menko, A. F. Pozharskii, and N. A. Klyuev, *Khim. Geterotsikl. Soedin.*, No. 9, 1226 (1988).
6. V. D. Orlov, Kh. Kiroga, N. N. Kolos, and S. M. Desenko, *Khim. Geterotsikl. Soedin.*, No. 7, 962 (1988).
7. V. D. Orlov, S. M. Desenko, and N. S. Pivnenko, *Khim. Geterotsikl. Soedin.*, No. 11, 1489 (1988).