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2-QUINAZOLYLGUANIDINES IN HETEROCYCLIZATION REACTIONS. 2*. CONDENSATION WITH α,β-UNSATURATED CARBONYL COMPOUNDS

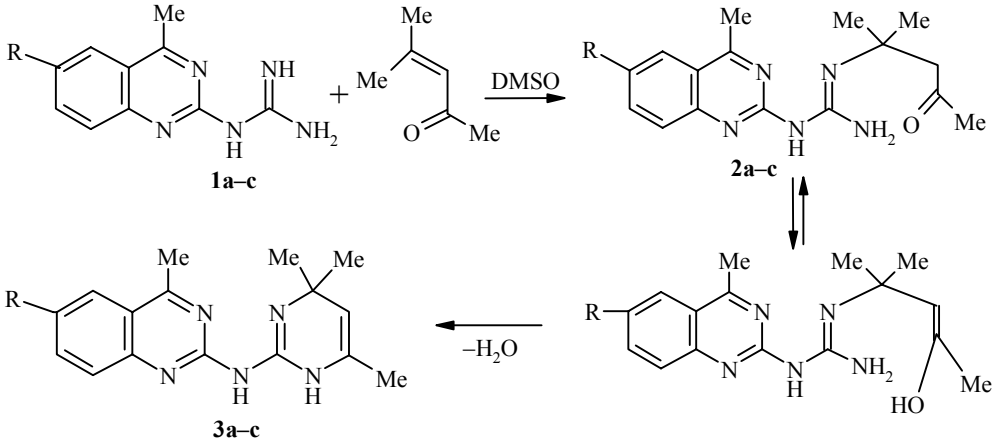
Kh. S. Shikhaliev, A. V. Falaleev, G. I. Ermolova, and A. S. Solov'ev

4,6,6-Trimethyl-1,4-dihydropyrimidines have been synthesized by condensation of 2-quinazolyl-guanidines with mesityl oxide. The analogous reaction with benzalacetone leads to unstable 4-methyl-6-phenyl-1,4-dihydropyrimidines, which are oxidized to the corresponding 4-methyl-6-phenylpyrimidines.

Keywords: 4-methyl-6-phenyl-1,4-dihydropyrimidines, 4-methyl-6-phenylpyrimidines, mesityl oxide, 4,6,6-trimethyl-1,4-dihydropyrimidines, 2-quinazolylguanidines, condensation, oxidation.

This report is devoted to study of cyclization of 6-R-4-methyl-2-quinazolylguanidines **1a-c** with α,β-unsaturated carbonyl compounds. Available data on the direction and especially the products of such a reaction with simple guanidines are contradictory [2-4].

It has been established that quinazolylguanidines **1a-c** easily react with mesityl oxide to form only a single product. Obviously the reaction begins with a Michael's addition of an imino group of compounds **1** at the β-position of the unsaturated bond of the mesityl oxide, with subsequent enolization of the intermediate guanidino ketones **2**, which in the last step undergo ring closure with removal of water to the final 6-R-4-methyl-2-(4,6,6-trimethyl-1,4-dihydropyrimidinyl-2-amino)quinazolines **3a-c**. The latter are stable to oxidation (aromatization) due to the presence of a *gem*-dimethyl group in the 4 position.



1-3 a R = H, **b** R = Me, **c** R = MeO

* For Communication 1, see [1].

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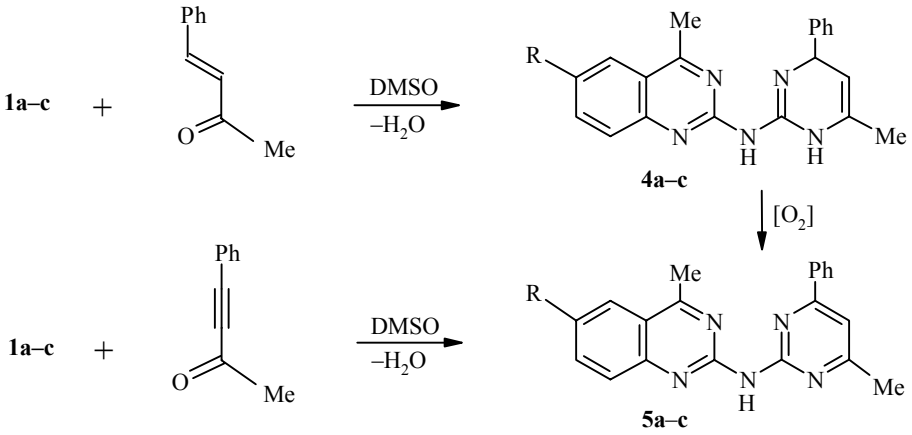
TABLE 1. Physicochemical and Spectral Characteristics of Substituted Dihydropyrimidinylaminoquinazolines **3a-c** and Pyrimidinylaminoquinazolines **5a-c**

Compound	Emperical formula	Found, % / Calculated, %				mp, °C	^{1}H NMR spectrum, δ, ppm	Yield, %
		M*	C	H	N			
3a	$C_{16}H_{19}N_5$	281 / 281.36	68.32 / 68.30	6.76 / 6.77	24.91 / 24.93	139-140	1.30 (6H, s, 4',4'-Me_2); 1.83 (3H, s, 6'-Me); 2.75 (3H, s, 4-Me); 4.42 (1H, s, 5'-H); 7.20-7.50 (4H, m, H_{arom}); 9.50 (2H, s, NH)	46
3b	$C_{17}H_{21}N_5$	295 / 295.39	69.15 / 69.14	7.12 / 7.13	23.73 / 23.75	183-184	1.30 (6H, s, 4',4'-Me_2); 1.85 (3H, s, 6'-Me); 2.41 (3H, s, 6-Me); 2.81 (3H, s, 4-Me); 4.41 (1H, 5'-H); 7.30-7.70 (3H, m, H_{arom}); 9.65 (2H, s, NH)	48
3c	$C_{17}H_{21}N_5O$	311 / 311.39	65.60 / 65.62	6.75 / 6.75	22.51 / 22.50	145-146	1.35 (6H, s, 4',4'-Me_2); 1.81 (3H, s, 6'-Me); 2.70 (3H, s, 4-Me); 3.90 (3H, s, OMe); 4.42 (1H, s, 5'-H); 7.20-7.50 (3H, m, H_{arom}); 9.60 (2H, s, NH)	51
5a	$C_{20}H_{17}N_5$	327 / 327.39	73.40 / 73.42	5.20 / 5.18	21.41 / 21.39	170-171	2.44 (3H, s, 6'-Me); 2.83 (3H, s, 4-Me); 7.40-8.30 (11H, m, H_{arom}); 9.60 (1H, s, NH)	47
5b	$C_{21}H_{19}N_5$	341 / 341.42	73.82 / 73.88	5.55 / 5.61	20.60 / 20.51	175-176	2.44 (3H, s, 6'-Me); 2.83 (3H, s, 4-Me); 2.41 (3H, s, 6-Me); 9.60 (1H, s, NH); 7.40-8.30 (10H, m, H_{arom})	40
5c	$C_{21}H_{19}N_5O$	357 / 357.42	70.59 / 70.61	5.32 / 5.30	19.61 / 19.59	102-104	2.45 (3H, s, 6'-Me); 2.85 (3H, s, 4-Me); 3.90 (3H, s, OMe); 9.62 (1H, s, NH); 7.40-8.30 (10H, m, H_{arom})	46

* By mass spectrometry.

Condensation of quinazolylguanidines **1a-c** with benzalacetone occurs *via* an analogous mechanism to form intermediate 1,4-dihydropyridinyl-2-amino-substituted quinazolines **4a-c**. But the latter, in contrast to products **3**, are unstable and even under the reaction conditions (dimethylsulfoxide, oxygen) are oxidized to the corresponding 6-R-4-methyl-2-(4-methyl-6-phenylpyrimidinyl-2-amino)quinazolines **5a-c**, which we synthesized also by reaction of quinazolylguanidines **1a-c** with 4-phenyl-2-butynone. The characteristics of the synthesized compounds are presented in Table 1.



4, 5 a R = H, **b** R = Me, **c** R = MeO

EXPERIMENTAL

The course of the reaction and the purity of the substances obtained were monitored by TLC on Silufol UV-254 plates (eluent: chloroform, ethylacetate). The ^{1}H NMR spectra were taken on a Bruker AC-300 (300 MHz) in DMSO-d_6, internal standard TMS. The mass spectra were taken on an LKB-9000, electron ionizing energy 70 eV.

The starting 6-R-4-methyl-2-quinazolylguanidines **1a-c** were synthesized according to the known procedure [5].

6-R-4-Methyl-2-(4,6,6-trimethyl-1,4-dihydropyrimidinyl-2-amino)quinazolines (3a-c). A mixture of quinazolylguanidine **1** (0.015 mol) and mesityl oxide (0.02 mol) in DMSO (40 ml) was held at 100°C for 12 h and then cooled down and poured into water. The precipitate was filtered off and recrystallized from methanol.

6-R-4-Methyl-2-(4-methyl-6-phenylpyrimidinyl-2-amino)quinazolines (5a-c). Benzalacetone (0.02 mol) was added to compound **1** (0.015 mol) in DMSO (40 ml). The mixture was held for 8-12 h at 100°C and then cooled down and poured into water. The precipitate was filtered off and dried. Product **5** was isolated from the precipitate by column chromatography on Al_2O_3 (eluent: chloroform) and was recrystallized from ethylacetate.

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