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SHORT COMMUNICATIONS

Synthesis of N^3,N^5,4-Triaryl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxamides

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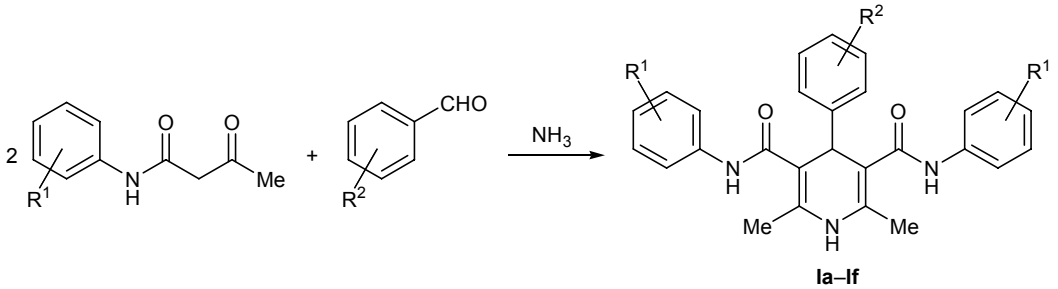
The known Hantzsch dihydropyridine synthesis is convenient for the preparation of 1,4-dihydropyridine derivatives having similar substituents in positions *2*/*6* and *3*/*5*. It is based on the reaction of β-keto ester with aldehyde and ammonia [1]. Modifications of this reaction were reported, where β-diketones, malonic acid esters, β-keto acids, β-aminocrotononitrile, ethyl cyanoacetate, and cyanoacetamide were used instead of β-keto esters [2]. While continuing studies in this field, we were the first to perform reactions of *N*-arylacetoacetamides with aromatic aldehydes and ammonia with a view to obtain new 1,4-dihydropyridine derivatives. The reactions were carried out by heating the reactants in boiling alcohol over a period of 3 h, and the products were the corresponding N^3,N^5,4-triaryl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxamides **Ia**–**If**.

Compounds **Ia**–**If** were isolated as light yellow crystalline substances which were soluble in DMF, DMSO, and hot ethanol and insoluble in water. The IR spectra of **Ia**–**If** contained absorption bands due to stretching vibrations of the amide carbonyl group (1656–1688 cm^{-1}), double C=C bonds (1600–1632 cm^{-1}), amide NH groups (3264–3312 cm^{-1}), and NH group in the pyridine ring (3348–3408 cm^{-1}). Compounds **Ia**–**If** displayed in the ^{1}H NMR spectra signals from protons in the aromatic rings and substituents therein, a six-proton singlet from two methyl groups (δ 2.24–2.45 ppm) a singlet from the 4-H proton in the pyridine ring (δ 4.84–5.05 ppm), a signal from the N^{1}H proton (δ 7.95–8.50 ppm), and a two-proton signal from amide NH groups (δ 9.21–9.25 ppm). In the mass spectrum of **Id** we observed the molecular ion peak and peaks of fragment ions which were consistent with the assumed structure.

2,6-Dimethyl-N^3,N^5,4-triphenyl-1,4-dihydropyridine-3,5-dicarboxamide (Ia). A mixture of 39 g (0.22 mol) of acetoacetanilide, 10.16 ml (0.1 mol) of benzaldehyde, 8 ml (0.11 mol) of concentrated aqueous ammonia, and 60 ml of ethanol was heated for 3 h under reflux, 40 ml of warm water was added, the mixture was cooled and treated with 60% aqueous ethanol, and the precipitate was filtered off and recrystallized from ethanol. Yield 6.5 g (15%), mp >300°C. IR spectrum, ν, cm^{-1}: 3408, 3272 (NH); 1680 (C=O); 1652 (C=C). ^{1}H NMR spectrum, δ, ppm: 2.02 s (6H, CH_3), 4.89 s (1H, 4-H), 7.03 m (15H, H_{arom}), 8.00 s



Ia–If

$R^1 = R^2 = H$ (**a**); R^1 = 2-MeO, $R^2 = H$ (**b**); $R^1 = H$, R^2 = 4-Cl (**c**); $R^1 = H$, R^2 = 3-O_2N (**d**); $R^1 = H$, R^2 = 4-O_2N (**e**); $R^1 = H$, R^2 = 2-Cl (**f**).

(1H, NH), 9.23 s (2H, NH). Found, %: C 76.37, 76.68; H 5.84, 5.99; N 9.65, 9.98. $C_{27}H_{25}N_3O_2$. Calculated, %: C 76.57; H 5.95; N 9.92.

Compounds **Ib**–**If** were synthesized in a similar way.

***N*³,*N*⁵-Bis(2-methoxyphenyl)-2,6-dimethyl-4-phenyl-1,4-dihydropyridine-3,5-dicarboxamide (Ib).** Yield 33%, mp 194–196°C. IR spectrum, ν, cm^{-1}: 3352, 3304 (NH); 1685 (C=O); 1648 (C=C). ^1H NMR spectrum, δ, ppm: 2.02 s (6H, CH_3), 3.64 s (6H, OCH_3), 4.95 s (1H, 4-H), 7.03 m (13H, H_{arom}), 8.43 s (1H, NH), 9.24 s (2H, NH). Found, %: C 72.14, 72.18; H 6.44, 6.29; N 8.65, 8.70. $C_{29}H_{29}N_3O_4$. Calculated, %: C 72.03; H 6.04; N 8.69.

4-(4-Chlorophenyl)-2,6-dimethyl-*N*³,*N*⁵-diphenyl-1,4-dihydropyridine-3,5-dicarboxamide (Ic). Yield 33%, mp 205–207°C. IR spectrum, ν, cm^{-1}: 3392, 3264 (NH); 1656 (C=O); 1648 (C=C). ^1H NMR spectrum, δ, ppm: 2.05 s (6H, CH_3), 5.09 s (1H, 4-H), 7.08 m (14H, H_{arom}), 8.50 s (1H, NH), 9.24 s (2H, NH). Found, %: C 71.04, 70.78; H 5.34, 5.31; N 9.15, 9.19. $C_{27}H_{24}ClN_3O_2$. Calculated, %: C 70.81; H 5.28; N 9.18.

2,6-Dimethyl-4-(3-nitrophenyl)-*N*³,*N*⁵-diphenyl-1,4-dihydropyridine-3,5-dicarboxamide (Id). Yield 39%, mp 205–207°C. IR spectrum, ν, cm^{-1}: 3440, 3304 (NH); 1680 (C=O); 1632 (C=C). ^1H NMR spectrum, δ, ppm: 2.07 s (6H, CH_3), 4.79 s (1H, 4-H), 7.07 m (14H, H_{arom}), 8.39 s (1H, NH), 9.25 s (2H, NH). Mass spectrum, *m*/*z*: 468 $[M - H]^+$, 451 $[M - NH_3]^+$, 376 $[M - PhNH]^+$, 346 $[M - C_6H_4NO_2]^+$, 93 $[M - PhNH_2]^+$, 77 $[M - Ph]^+$. Found, %: C 69.42, 69.36; H 5.04, 5.11; N 11.85, 11.92. $C_{27}H_{24}N_4O_4$. Calculated, %: C 69.22; H 5.16; N 11.96.

2,6-Dimethyl-4-(4-nitrophenyl)-*N*³,*N*⁵-diphenyl-1,4-dihydropyridine-3,5-dicarboxamide (Ie). Yield 45%, mp >300°C. IR spectrum, ν, cm^{-1}: 3420, 3312 (NH); 1670 (C=O); 1632 (C=C). ^1H NMR spectrum, δ, ppm: 2.06 s (6H, CH_3), 5.79 s (1H, 4-H), 7.07 m (14H, H_{arom}), 8.44 s (1H, NH), 9.25 s (2H, NH). Found, %: C 69.42, 69.36; H 5.04, 5.11; N 11.85, 11.92. $C_{27}H_{24}N_4O_4$. Calculated, %: C 69.22; H 5.16; N 11.96.

4-(2-Chlorophenyl)-2,6-dimethyl-*N*³,*N*⁵-diphenyl-1,4-dihydropyridine-3,5-carboxamide (If). Yield 31%, mp 215–217°C. IR spectrum, ν, cm^{-1}: 3432, 3304 (NH); 1680 (C=O); 1632 (C=C). ^1H NMR spectrum, δ, ppm: 2.04 s (6H, CH_3), 5.49 s (1H, 4-H), 7.06 m (14H, H_{arom}), 8.44 s (1H, NH), 9.24 s (2H, NH). Found, %: C 71.04, 70.78; H 5.34, 5.31; N 9.15, 9.19. $C_{27}H_{24}ClN_3O_2$. Calculated, %: C 70.81; H 5.28; N 9.18.

The IR spectra were recorded in mineral oil on a Specord M-80 spectrometer. The ^1H NMR spectra were measured relative to TMS on a Bruker DRX-500 instrument at 500.13 MHz using DMSO-d_6 as solvent. The mass spectrum of **Id** (electron impact, 70 eV) was obtained on a Finnigan MAT INCOS-50 instrument.

REFERENCES

1. Sagitullina, G.P., Glidzinskaya, G.V., Sitnikov, G.V., and Sagitullin, R.S., *Khim. Geterotsikl. Soedin*., 2002, p. 1518.
2. Matern, A.I., Charushin, V.N., and Chupakhin, O.N., *Usp. Khim*., 2007, vol. 76, p. 27.