

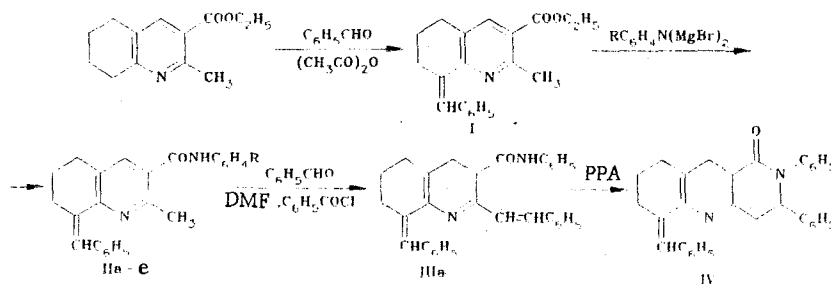
SYNTHESIS AND REACTIONS OF 8-BENZYLIDENE-2-METHYL-5,6,7,8-TETRAHYDROQUINOLINE-3-CARBOXYLIC ACID ARYLAMIDES

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Arylamides of 8-benzylidene-2-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid were obtained by treating the ethyl ester with dimagnesiumamines. An example is given of their conversion to 8-benzylidene-2-styryl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid anilides and subsequent cyclization to 1-oxo-1,2,3,4,6,7,8,9-octahydrobenzo[b]-1,6-naphthyridines.

We have previously [1] reported 2-styrylnicotinic acid amides and their conversion to 5-oxo-5,6,7,8-tetrahydro-1,6-naphthyridines. In order to extend this work it was of interest to synthesize 2-styryl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid arylamides. With this in mind, the chosen starting materials were ethyl 2-styryl-5,6,7,8-tetrahydroquinoline-3-carboxylate and dimagnesiumamines. Attempts to synthesize the former were made by heating ethyl 2-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylate and benzaldehyde in acetic anhydride using the method previously described [2] for 2-(*m*-nitrosyryl)-5,6,7,8-tetrahydroquinoline-3-carboxylic acid esters. The PMR spectrum of the reaction product showed signals as follows (δ in ppm): 1.17 (3H, carbethoxy CH_3), 1.5 (2H, CH_2 at position 6), 2.5 (4H, CH_2 at 5 and 7), 2.8 (3H, CH_3 at 2), 4.1 (carbethoxy CH_2), and 7.6 (7H, benzene and pyridine rings and benzylidene CH). Thus the compound obtained was ethyl 8-benzylidene-2-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylate (I).



Treatment of I with arylmagnesium halides gave 8-benzylidene-2-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid arylamides (IIa-e) in 80-90% yields (Table 1).

Compounds IIa-e were colorless, crystalline materials soluble in hot alcohol and dimethyl sulfoxide but insoluble in water and ether. The PMR spectrum of anilide IIa showed the following signals (δ in ppm): 1.3 and 2.3 (6H, polymethylenes), 2.7 (3H, CH_3), and 7.6 (12H, benzene and pyridine rings and benzylidene CH). A low field signal was also observed at 10.7 ppm due to the amido NH proton. The UV spectrum of IIa showed band maxima at 230, 275 and 330 nm.

Heating arylamides IIa,b with benzaldehyde in DMF in the presence of benzoyl chloride gave 8-benzylidene-2-styryl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid arylamides (IIIa,b). IIIa underwent cyclization when heated with polyphosphoric acid (PPA) to give 6-benzylidene-1-oxo-2,3-diphenyl-1,2,3,4,6,7,8,9-octahydrobenzo-[b]-1,6-naphthyridine (IV). The IR spectrum of IV shows the presence of a $\text{C}=\text{O}$ absorption band at 1650 cm^{-1} and absence of the amide N-H band seen in the arylamide IIIa. The PMR spectrum of IV showed the following signals (δ in ppm): 1.85, 2.8 (6H, protons at C_7 , C_8 and C_9), 3.67 (2H, $\text{H}-\text{C}_4$), 5.1 (1H, $\text{H}-\text{C}_3$), 8.0 (1H, $\text{H}-\text{C}_{10}$), and a multiplet centered at 7.2 ppm (16H, protons of the aromatic rings and the benzylidene CH).

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TABLE 1. 2-Methyl-8-benzylidene-5,6,7,8-tetrahydroquinoline-3-carboxylic Acid Anilides (IIa-e)

Compound	R	mp, °C	Found, %			Empirical formula	Calculated, %			Yield, %
			C	H(Br)	N		C	H(Br)	N	
IIa	H	209-210	80.0	6.2	7.9	C ₂₄ H ₂₂ N ₂ O	80.0	6.2	7.9	85
IIb	<i>m</i> -CH ₃	200-201	81.3	6.4	7.9	C ₂₅ H ₂₄ N ₂ O	81.5	6.5	7.6	81
IIc	<i>p</i> -CH ₃	218-219.5	81.4	6.5	7.6	C ₂₅ H ₂₄ N ₂ O	81.5	6.5	7.6	80
IId	<i>p</i> -CH ₃ O	235-236	78.0	6.6	7.5	C ₂₅ H ₂₄ N ₂ O ₂	78.1	6.3	7.3	90
IIe	<i>p</i> -Br	232-232.5	—	(18.3)	6.7	C ₂₄ H ₂₁ BrN ₂ O	—	(18.5)	6.5	83

EXPERIMENTAL

IR spectra were recorded on a UR-20 instrument (GDR) in paraffin oil and PMR spectra on an RYa-2310 (60 MHz) with HMDS as internal standard. UV spectra were obtained with an SF-16 using ethanol solvent at concentrations of 10⁻⁵ M.

Ethyl 8-benzylidene-2-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylate (I). A mixture of ethyl 2-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylate [3] (1.4 g, 4.5 mmoles) and benzaldehyde (0.61 g, 5.8 mmoles) in acetic anhydride (1 ml) were heated in a metal bath at 130°C for 3 h. After cooling the product was triturated with a small amount of ether, the precipitate filtered off and crystallized from ethanol. The yield was 0.84 g (60%) with mp 121-122°C. Found: C 78.3; H 6.7; N 4.4%. C₂₀H₂₁NO₂. Calculated: C 78.2; H 6.8; N 4.6%.

8-Benzylidene-2-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylic acid Arylamides (IIa-e, Table 1). Ethyl 8-benzylidene-2-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylate (60 mmoles) in anhydrous ether (20 ml) was added to the dimagnesiumamine (previously prepared from the corresponding arylamine (90 mmoles) and ethylmagnesium bromide (180 mmoles) in ether). The mixture was heated for 0.5 h and then decomposed using saturated ammonium chloride. The ether layer was separated, steam distilled and the residue crystallized from ethanol.

8-Benzylidene-2-styryl-5,6,7,8-tetrahydroquinoline-3-carboxylic Acid Anilide (IIIa). A solution containing IIa (0.5 g, 1.4 mmoles), benzoyl chloride (0.3 g, 2.1 mmoles), freshly distilled benzaldehyde (0.2 g, 1.8 mmoles) and DMF (5 ml) was heated for 16 h at 185-190°C. Decomposition with conc. HCl and steam distillation yielded hydrolyzed benzoic acid and benzaldehyde and the residue in the distillation flask was recrystallized from ethanol. The yield was 0.37 g (60%) with mp 255-257°C. Found: C 84.1; H 6.0; N 6.2%. C₃₁H₂₆N₂O. Calculated: C 84.2; H 5.9; N 6.1%. Compound IIIb was obtained analogously in 52% yield, mp 228-230°C (ethanol). Found: C 84.3; H 6.0; N 6.1%. C₃₂H₂₈N₂O. Calculated: C 84.2; H 6.1; N 6.1%.

6-Benzylidene-1-oxo-2,3-diphenyl-1,2,3,4,6,7,8,9-octahydrobenzo[b]-1,6-naphthyridine (IV). A mixture of IIIa (0.12 g mmole) and polyphosphoric acid (containing 80-84% P₂O₅) were heated at 135°C for 3 h. The product was poured into iced water (30 ml), the acid layer neutralized (Na₂CO₃) and the resulting solid crystallized from ethanol. The yield was 0.1 g (90%) with mp 178-180°C. Found: C 84.3; H 5.7; N 6.1%. C₃₁H₂₆N₂O. Calculated: 84.2; H 5.9; N 6.3%.

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