1-ACYL-3-ARYLAZOINDOLES IN THE SYNTHESIS OF INDOLO[1,2-c]QUINAZOLINES

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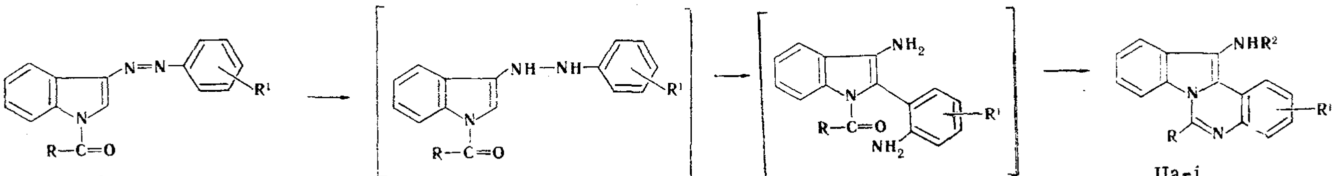
Treatment of 1-acyl-3-arylazoindoles with zinc in acetic acid in the presence of acetic anhydride and sodium acetate leads to 12-acetamidoindolo[1,2-c]quinazolines. 12-Aminoindolo[1,2-c]quinazolines are obtained when the reaction is carried out in the absence of acetic anhydride and sodium acetate.

We have found that 1-acyl-3-arylazoindoles (Ia-f) form 12-acetamidoindolo[1,2-c]quinazolines (IIa-f) when they are reduced with zinc in acetic acid in the presence of acetic anhydride and sodium acetate. The reaction evidently proceeds through a step involving the formation of hydrazo derivatives, which, like 3-arylhydrazoindoles that do not contain a substituent attached to the nitrogen atom of the indole ring [1], undergo a rearrangement of the benzidine type, as a result of which 2-(o-aminoaryl)-3-aminoindoles, which are subsequently cyclized to indoloquinazolines (IIa-f), are formed.



Ia-f

IIa-i

12-Aminoindolo[1,2-c]quinazolines (IIg-i) are formed by the action of zinc in acetic acid on 1-acyl-3-arylazoindoles (Ia,b,f).

The structures of the products were confirmed by the identical character of their UV spectra and by the absence of melting-point depressions for mixtures of samples of IIa-c,g with authentic samples of these substances, which we previously synthesized by a different method [1].

EXPERIMENTAL

1-Acetyl-3-arylazoindoles (Ia-d). A solution of 0.05 mole of the 3-arylazoindole in 25 ml of acetic anhydride was refluxed for 20 min, after which it was cooled, and the resulting precipitate was removed by filtration, washed with methanol, and dried. Data on Ia-d are presented in Table 1.

1-Phenylacetyl-3-phenylazoindole (Ie). A 7-ml (0.05 mole) sample of triethylamine was added to a solution of 11 g (0.05 mole) of 3-phenylazoindole in 100 ml of absolute dioxane, the mixture was cooled, and 6.6 ml (0.05 mole) of phenylacetyl chloride was added dropwise. The resulting precipitate was removed by filtration and washed with dioxane. The mother liquor was diluted with water, and the liberated oil began to crystallize on standing. The solid material was removed by filtration and triturated with methanol. The yield of product with mp 121.5-122.5° (from methanol) was 4.4 g (26%). Found: C 77.6; H 4.9; N 12.6%. $C_{22}H_{17}N_3O$. Calculated: C 77.9; H 5.1; N 12.4%.

1-Benzoyl-3-phenylazoindole (If). A 5.7-ml (0.05 mole) sample of benzoyl chloride was added dropwise with cooling to a solution of 11 g (0.05 mole) of 3-phenylazoindole in 50 ml of dry pyridine. At the end of the addition, the mixture was stirred at room temperature for

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TABLE 1. 1-Acetyl-3-arylazoindoles (Ia-d)

Compound	R¹	mp, °C (from methanol	Found, %			Empirical formula	Calc., %			Yield, %
			C	H	N		C	H	N	
Ia	H	154—155	72,9	5,2	15,8	$C_{16}H_{13}N_3O$	73,0	5,0	16,0	97,7
Ib	o-CH_3	135—136	74,0	5,6	15,3	$C_{17}H_{15}N_3O$	73,6	5,5	15,2	93
Ic	p-CH_3	173—174	74,0	5,4	15,2	$C_{17}H_{15}N_3O$	73,6	5,5	15,2	85,6
Id	p-$COOC_2H_5$	184—185	68,7	5,2	12,6	$C_{19}H_{17}N_3O_3$	68,1	5,1	12,5	91

TABLE 2. Indolo[1,2-c]quinazolines (IIa-i)

Compound	R	R¹	R²	mp, °C	Found, %			Empirical formula	Calc., %			Yield, %
					C	H	N		C	H	N	
IIa	CH_3	H	CH_3CO (dec.)	304—305[a] (dec.)	74,9	5,3	14,5	$C_{18}H_{15}N_3O$	74,7	5,2	14.5	70
IIb	CH_3	2-CH_3	CH_3CO	316—318[a] (dec.)	75,2	5,9	13,8	$C_{19}H_{17}N_3O$	75,2	5,7	13,9	70
IIc	CH_3	4-CH_3	CH_3CO	298—300[a] (dec.)	75,5	5,7	13,9	$C_{19}H_{17}N_3O$	75,2	5,7	13,9	63,3
IId	CH_3	2-$COOC_2H_5$	CH_3CO	289—290[a]	69,5	5,2	11,5	$C_{21}H_{19}N_3O_3$	69,8	5,3	11,6	22,2
IIe	$CH_2C_6H_5$	H	CH_3CO	283,5—285,5[a] (dec.)	79,2	5,4	11,4	$C_{24}H_{19}N_3O$	78,9	5,2	11,5	83,3
IIf	C_6H_5	H	CH_3CO	315—316,5 (dec.)	78,9	4,9	12,1	$C_{23}H_{17}N_3O$	78,6	4,9	12,0	77
IIg	CH_3	H	H	202,5—204[b] (dec.)	78,1	5,0	17,0	$C_{16}H_{13}N_3$	77,7	5,3	17,0	72,8
IIh	CH_3	4-CH_3	H	173—173,5[c]	78,4	5,6	16,2	$C_{17}H_{15}N_3$	78,1	5,8	16,1	57,7
IIi	C_6H_5	H	H	dec.>300[b]	81,3	5,1	13,5	$C_{21}H_{15}N_3$	81,5	4,9	13,6	90,6

[a] From dimethylformamide. [b] From methanol. [c] From methanol–dimethylformamide (3:1).

1 h, after which it was poured into water. The resulting precipitate was removed by filtration, washed with water and methanol, and dried to give 16.2 g (quantitative yield) of a product with mp 150-151° (from methanol). Found: C 77.7; H 4.6; N 12.9%. $C_{12}H_{15}N_3O$. Calculated: C 77.5; H 4.7; N 12.9%.

12-Acetamidoindolo[1,2-c]quinazolines (IIa-f). A 0.014-mole sample of fused sodium acetate, 0.01 mole of acetic anhydride, and, in portions, 0.06 mole of zinc dust were added successively to a suspension of 0.01 mole of 1-acyl-3-arylazoindole (Ia-f) in 30 ml of glacial acetic acid while maintaining the temperature of the mixture at 55-60°. The mixture was then stirred for 30 min as the temperature gradually was lowered to room temperature. The resulting precipitate was removed by filtration and refluxed with dimethylformamide. The insoluble residue was removed by filtration, and mother liquor was cooled and diluted with water. The resulting precipitate was removed by filtration, washed with methanol, and dried. Data on IIa-f are presented in Table 2.

12-Aminoindolo[1,2-c]quinazolines (IIg-i). Zinc dust was added in portions to a suspension of 0.01 mole of 1-acetyl-3-arylazoindole (Ia,b) in 30 ml of glacial acetic acid while maintaining the temperature of the mixture at 55-60°. At the end of the addition, the mixture was stirred for 30 min as the temperature was lowered to room temperature. Distilled water (∿200 ml) was added to the mixture, the sludge was removed by filtration, and filtrate was cooled and made alkaline with excess concentrated ammonium hydroxide. The precipitate was removed by filtration, washed with water and methanol, and dried. Data on IIg,h are presented in Table 2. 12-Aminoindolo[1,2-c]quinazoline IIi was similarly obtained from If, except that at the end of the reaction the residue was removed by filtration and washed with glacial acetic acid, and the filtrate was poured into water. The resulting precipitate was removed by filtration, washed with water, and dried. Data on IIi are presented in Table 2.

LITERATURE CITED

1. V. I. Shvedov, G. N. Kurilo, A. A. Cherkasova, and A. N. Grinev, Khim. Geterotsikl. Soedin., No. 8, 1096 (1975).