LITERATURE CITED

1. N. Yu. Kuz'mina, D. V. Sokolov, and G. S. Litvinenko, Izv. Akad. Nauk Kaz. SSR, Ser. Khim., No. 4, 70 (1986).
2. K. I. Khludneva, G. S. Litvinenko, and D. V. Sokolov, The Chemistry of Natural and Biologically Active Substances in Kazakhstan [in Russian], Nauka, Alma-Ata (1967), p. 3.
3. G. S. Litvinenko, V. V. Sosnova, and D. V. Sokolov, Izv. Akad. Nauk Kaz. SSR, Ser. Khim., No. 1, 37 (1973).
4. G. S. Litvinenko, V. V. Sosnova, and D. V. Sokolov, Izv. Akad. Nauk Kaz. SSR, Ser. Khim., No. 2, 47 (1973).
5. C. A. Grob and H. J. Lutz, Helv. Chim. Acta, 48, 791 (1965).
6. J. A. Marshall and J. H. Bobler, J. Org. Chem., 34, 4186 (1969).
7. É. A. Mistryukov and V. F. Kucherov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk No. 7, 1343 (1961); No. 9, 1816.
8. É. A. Mistryukov, N. I. Aronova, and V. F. Kucherova, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, No. 8, 1599 (1962).
9. G. T. Katvalyan and É. A. Mistryukov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 12, 2575 (1968).
10. G. T. Katvalyan and É. A. Mistryukov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 9, 1809 (1969).
11. D. V. Sokolov, K. I. Khludneva, T. B. Volkova, and G. S. Litvinenko, Izv. Akad. Nauk Kaz. SSR, Ser. Khim., No. 2, 78 (1976).
12. É. A. Mistryukov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, No. 5, 929 (1963).
13. É. A. Mistryukov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 9, 1826 (1965).
14. W. Hückel and F. Stepf, Ann., 453, 171 (1927).
15. L. Van den Enden, H. J. Geise, and A. Spelbos, J. Mol. Struct., 44, 177 (1978).
16. K. D. Hargrave and E. L. Eliel, Israel J. Chem., 20, 127 (1980).
17. I. N. Nazarov and É. A. Mistryukov, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, No. 3, 584 (1958).
18. R. G. Gerr, A. I. Yanovskii, and Yu. T. Struchkov, Kristallografiya, No. 10, 1029 (1983).

SYNTHESIS AND REACTIONS OF 3-(N-ARYLCARBAMOYL)-2-METHYLCINCHONINIC ACID

S. V. Ukhov and M. E. Konshin

UDC 547.756'831.9'832.5

The Pfitzinger reaction between acetoacetic acid arylamides and the potassium salt of isatinic acid leads in good yield to 3-(N-arylcarbamoyl)-2-methylcinchoninic acids. Refluxing the latter in 2-propanol produced N-substituted imides of 2-methylquinoline-3,4-dicarboxylic acids and, with benzaldehyde in p-xylene in the presence of piperidine, to N-phenylimides of 2-styrylquinoline-3,4-dicarboxylic acids.

The Pfitzinger reaction finds widespread usage in the synthesis of quinoline-4-carboxylic acids [1] but there has only been one application of this method to quinoline-3,4-dicarboxylic acids [1, 2].

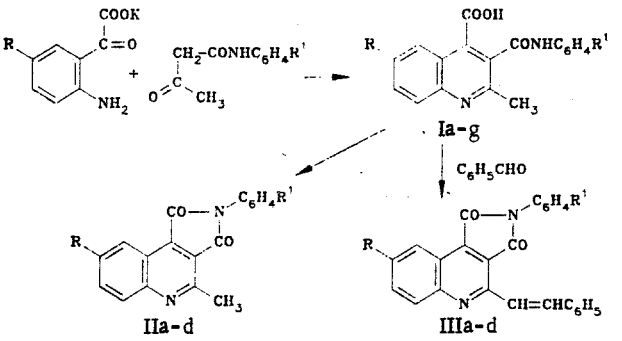
Experiments have shown that 3-(N-arylcarbamoyl)-2-methylcinchoninic acids (Ia-g, Table 1) are formed in good yields by treating the potassium salt of isatinic acids with acetoacetic acid arylamides.

Perm State Pharmaceutical Institute, Perm 614600. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 652-653, May, 1988. Original article submitted November 26, 1986; revision submitted March 31, 1987.

0009-3122/88/2405-0531$12.50

TABLE 1. Parameters for Synthesized Compounds

Compound	mp, °C	Found, %				Empirical formula	Calculated, %				Yield, %
		C	H	Hal	N		C	H	Hal	N	
Ia	193—195	70,8	4,7	—	9,0	$C_{18}H_{14}N_2O_3$	70,6	4,6	—	9,2	82
Ib	214—216	—	—	21,1	7,1	$C_{18}H_{13}BrN_2O_3$	—	—	20,8	7,3	77
Ic	207—209	—	—	10,1	8,3	$C_{18}H_{13}ClN_2O_3$	—	—	10,4	8,2	87
Id	203—204	71,4	5,2	—	9,1	$C_{19}H_{16}N_2O_3$	71,3	5,0	—	8,8	88
Ie	187—189	61,7	4,0	—	12,1	$C_{18}H_{13}N_3O_5$	61,5	3,7	—	12,0	55
If	168—170	71,5	5,1	—	9,0	$C_{19}H_{16}N_2O_3$	71,3	5,0	—	8,8	57
Ig	222—223	68,1	4,9	—	8,6	$C_{19}H_{16}N_2O_4$	67,9	4,8	—	8,3	44
IIa	161—163	75,3	4,3	—	10,0	$C_{18}H_{12}N_2O_2$	75,0	4,2	—	9,7	95
IIb	178—180	—	—	21,9	7,6	$C_{18}H_{11}BrN_2O_2$	—	—	21,8	7,6	93
IIc	173—174	—	—	11,0	8,6	$C_{18}H_{11}ClN_2O_2$	—	—	11,0	8,7	93
IId	150—151	75,6	4,8	—	9,6	$C_{19}H_{14}N_2O_2$	75,5	4,6	—	9,3	95
IIIa	239—241	80,0	4,4	—	7,7	$C_{25}H_{16}N_2O_2$	79,8	4,2	—	7,4	75
IIIb	267—269	—	—	17,7	6,4	$C_{25}H_{15}BrN_2O_2$	—	—	17,6	6,2	43
IIIc	252—254	—	—	8,8	7,0	$C_{25}H_{15}ClN_2O_2$	—	—	8,6	6,8	50
IIId	237—239	80,3	4,8	—	7,3	$C_{26}H_{18}N_2O_2$	80,0	4,6	—	7,2	46
IIIe	270—271	—	—	—	9,8	$C_{25}H_{15}N_3O_4$	71,3	3,6	—	10,0	65



I—III a,f,g R=H, b R=Br, c R=Cl, d R=CH_3, e R=NO_2, a-e R^1=H, f R^1=*p*-CH_3, g R^1=*p*-CH_3O

The IR spectra of Ia-g show bands at 1670-1680 (CO) and 3320-3340 cm^{-1} (NH). The PMR spectra show a singlet for the methyl groups at 2.6, a multiplet for the atomatic protons and the carboxyl OH centered at 7.4, and a broad signal for the amide NH protons at 10.36 ppm.

Refluxing the anilides Ia-d in isopropanol causes cyclization to the N-arylimides of 2-methylquinoline-3,4-dicarboxylic acids, IIa-d. In contrast to Ia-d the IR spectra of IIa-d show the absence of the absorption at 3320-3340 cm^{-1} and a single CO absorption at 1700-1710 cm^{-1}. In their PMR spectra the methyl group singlet is at 2.78 ppm and the aromatic protons are centered at 7.85 ppm.

Bearing in mind that the methyl group in amides Ia-g would behave as CH acids we have subjected these compounds to reaction with benzaldehyde (and with furfural in the case of amide Ic) by heating with catalytic amounts of piperidine. Cyclization occurs to N-arylimides of 2-styrylquinoline-3,4-dicarboxylic acids. The products (IIIa-f) showed IR bands at 1700-1710 cm^{-1} (CO) and PMR multiplet signals centered at 7.1-7.5 ppm (H arom and CH=CH groups).

The UV spectra of imides IIa-d show maxima at 260 nm whereas IIIa-f have a diffuse absorption in the region 260-340 nm with weakly defined minima and maxima which points to increase in system conjugation in the latter.

EXPERIMENTAL

IR spectra were recorded on a UR-20 for paraffin mulls. PMR spectra were obtained on an NR-2310 (60 MHz) instrument using DMSO-d_6 solvent (5%) and HMDS internal standard. UV spectra were taken on an SF-16 spectrometer for 10^{-5} M solutions in ethanol.

3-N-Arylcarbamoyl-2-methylcinchoninic Acids (Ia-g). Acetoacetic acid arylamides (10 mmole) in ethanol (10 ml) were added to a solution of isatin (or its 5-substituted derivative) (10 mmole) and potassium hydroxide (0.56 g, 10 mmole) in ethanol (10 ml). After

refluxing for 7 h, the product was diluted with water (10 ml), acidified with acetic acid, the precipitated solid filtered off, and crystallized from DMF.

2-Methylquinoline-3,4-dicarboxylic Acid N-Phenylimides (IIa-d). A solution of Ia-d (3 mmole) in isopropanol (50 ml) was refluxed for 4 h, cooled, and the precipitate filtered off to give the desired product.

2-Methylquinoline-3,4-dicarboxylic Acid N-Phenylimide (IIa). A solution of Ia (1 g, 3 mmole) in acetic anhydride (5 ml) was refluxed for 2 h, poured into water (50 ml), and the precipitated solid filtered off and crystallized from ethanol to give IIa (0.5 g, 53%) with mp 161-163°C. A mixed melting point with a sample of IIa prepared as described before was not depressed.

2-Styrylquinoline-3,4-dicarboxylic Acid N-Phenylimides (IIIa-e). A mixture of anilide Ia-e (7 mmole), benzaldehyde (1.06 g, 10 mmole), p-xylene (2 ml), and piperidine (3-4 drops) was heated at 175°C in a metal bath for 5 h. The product was crystallized from ethyl acetate.

Under the same conditions, compound Ic (4 g, 11 mmole) and furfural (1.63 g, 17 mmole) gave 2-[2-(α-furyl)vinyl]-6-chloroquinoline-3,4-dicarboxylic acid N-phenylimide (4 g, 80%) with mp 263-265°C (ethyl acetate). Found: Cl 8.6; N 7.2%. $C_{23}H_{13}ClN_2O_3$. Calculated: Cl 8.8; N 7.0%.

LITERATURE CITED

1. R. Elderfield, Heterocyclic Compounds, Vol. 4, Wiley, New York (1954).
2. E. Campaigne and J. Hutchinson, J. Heterocyclic. Chem., 7, 655 (1970).

ACYLATION OF 2- AND 4-HYDROXYAMINOPYRIMIDINES

V. F. Sedova, G. G. Moskalenko, and V. P. Mamaev*

UDC 547.853.7:542.951.1

Monoacylation of alkyl (aryl)-containing 2- and 4-hydroxyaminopyrimidines with acid anhydrides and acid chlorides leads preferentially to the acyloxyaminopyrimidines; the corresponding reaction with isocyanates leads to the (N-carbamoyl)hydroxyaminopyrimidines.

The exhaustive acylation of N-aryl (hetaryl)hydroxylamines leads to N,O-diacylhydroxylamines [1], the stability of which depends on the structure of the acyl group [2]. The monoacylation of N-aryl (hetaryl)hydroxylamines proceeds preferentially at the nitrogen atom with the formation of the N-aryl (hetaryl)-N-acylhydroxylamines [1], and the acylation at the oxygen atom is only observed in the case of acceptor or sterically hindered aryl substituents [2]. The O-acylhydroxylamines are unstable compounds [2-5], which undergo a series of conversions via the intermediate nitrenium ions [4].

We investigated the acylation of 2- and 4-hydroxyaminopyrimidines with acid anhydrides and acid chlorides, and isocyanates, to explain the influence of the pyrimidinyl substituent on the properties of the hydroxyamino group. It is known that the corresponding O-acyl derivatives are formed by the acylation of 2-hydroxy-4-hydroxyamino-5-fluoropyrimidine with acetic anhydride, and of 6-hydroxyamino-1,3-dimethyluracil with ethyl isocyanate [7, 8].

We obtained the 4-(N-acetyl-N-acetoxy)amino-6-methyl-2-phenyl- and 4-(N-acetyl-N-acetoxy)amino-2,6-diphenylpyrimidines (IIa, b) by the action of an excess of acetic anhydride

*Deceased.

Novosibirsk Section, All-Union Scientific Research Institute of Chemical Agents of Plant Protection, Novosibirsk 630090. Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Academy of Sciences of the USSR, Novosibirsk 630090.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 654-658, May, 1988. Original article submitted November 20, 1986.