HETEROCYCLES, Vol 12, No 2, 1979

A SYNTHESIS OF 3-HYDROXYIMINOACYL-4-QUINAZOLINES AND TRANSFORMATION INTO 1,2,4-OXADIAZOLES

Katsuhiko Nagahara* and Atsushi Takada
School of Pharmaceutical Sciences, Kitasato University,
Shirokane, Minato-ku, Tokyo 108, Japan

Treatment of N-hydroxyiminobenzyl-2-aminobenzamides (I) with ortho esters afforded the corresponding 2-alkyl-3-hydroxyiminoacyl-4-quinazolones (II) and 3,5-diaryl-1,2,4-oxadiazoles (III), respectively. Furthermore, treatment of II with ethanolic hydrochloric acid caused the ring transformation to give the corresponding III.

We have recently described that the alkali hydrolysis or the pyrolysis of N-hydroxyiminobenzyl-2-aminobenzamides gives the corresponding 3,5-diaryl-1,2,4-oxadiazole derivatives.[1] We now report should be syntheses of 2-alkyl-3-hydroxyiminoacyl-4-quinazolones (II) by reaction of N-hydroxyiminobenzyl-2-aminobenzamides (I) with ortho esters as well as a new ring transformation of II to 1,2,4-oxadiazoles (III).

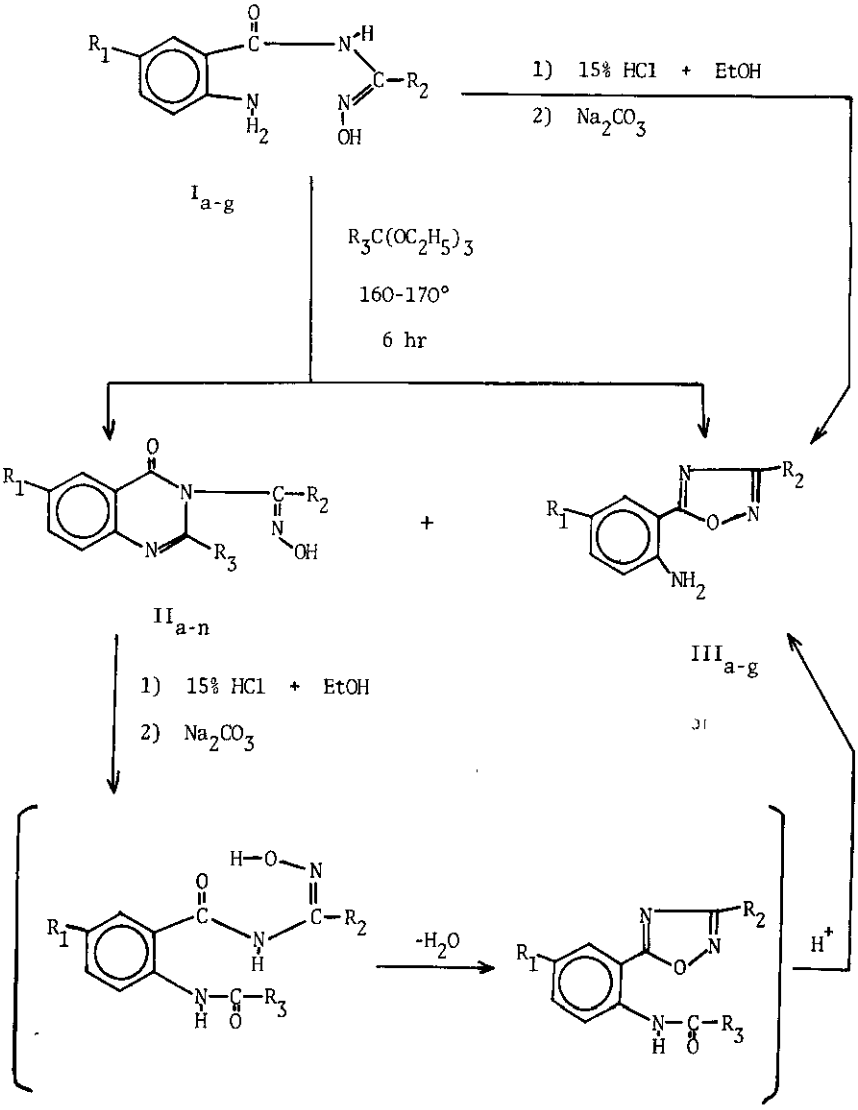
Treatment of (Ia-g)(0.0078 mol) with triethyl orthoacetate (or triethyl orthopropionate)(25 ml) at 160-170° for 6 hr afforded 3,4-dihydro-4-oxoquinazoline derivatives in good yields, which were previously unknown, i.e., 2-alkyl-3-hydroxyiminoacyl-4-quinazolonenes (IIa-n), and a trace amount of 3,5-diaryl-1,2,4-oxadiazoles (IIIa-g)[2]. The compounds (II)[3,4] were isolated by evaporation of the reaction mixture and addition of petroleum benzine and water, while the compounds (III)[5] were detected by TLC from the filtrate removed II (Table I).

Next, refluxing of (IIa-n)(0.003 mol) with a mixture of 15% hydrochloric acid (30 ml) and ethanol (30 ml) for 8 hr afforded

IIIa-g in good yields (Table II).

On the contrary, treatment of Ia-b with a mixture of 15% hydrochloric acid and ethanol under the same conditions provided IIIa-b, albeit in low yields (5%).

The ring transformation of II to III probably proceeds by initial hydrolysis of the pyrimidine nucleus and subsequent dehydration.



Scheme

Table I 4-Quinazolones (II)

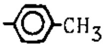
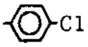
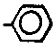
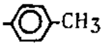
Starting material			R_3	Product	Mp(°C)	Recrystn. solvent	Yield(%)
	R_1	R_2					
Ia	H		CH_3	IIa	245-247	EtOH-H_2O	62
			C_2H_5	IIb	236-237	EtOH-H_2O	70
Ib	H		CH_3	IIc	235-237	EtOH-H_2O	57
			C_2H_5	IId	223-225	DMF-H_2O	98
Ic	H		CH_3	IIe	241-243	EtOH-H_2O	68
			C_2H_5	IIf	255-256	EtOH-H_2O	62
Id	Cl		CH_3	IIg	218-219	EtOH-H_2O	50
			C_2H_5	IIh	226-228	EtOH-H_2O	71
Ie	Cl		CH_3	IIi	245-246	EtOH-H_2O	56
			C_2H_5	IIj	228-229	EtOH-H_2O	54
If	H		CH_3	IIk	233-235	DMF-H_2O	35
			C_2H_5	IIl	245-246	DMF-H_2O	46
Ig	Cl		CH_3	IIm	236-238	DMF-H_2O	31
			C_2H_5	IIn	222-224	DMF-H_2O	36

Table II 1,2,4-Oxadiazoles (III)

Starting material	Product[a]	Mp(°C)	Yield(%)
IIa	IIIa	130-132[b]	68
IIb	IIIa	130-132	66
IIc	IIIb	151-152[c]	81
IId	IIIb	151-152	80
IIe	IIIc	150-151	75
IIf	IIIc	150-151	78
IIg	IIId	183-185[d]	86
IIh	IIId	183-185	83
IIi	IIIe	195-197	84
IIj	IIIe	194-196	92
IIk	IIIf	164-165	86
IIl	IIIf	164-165	88
IIm	IIIg	200-201	81
IIn	IIIg	200-202	66

a) All products were recrystallized from ethanol.

b) Lit.[1] 131-132°. c) Lit.[1] 152-153°. d) Lit.[1] 180-181°.

ACKNOWLEDGEMENT The author wish to thank Miss Noriko Ishiguro, the student of Kitasato University, for her skilled technical assistance, and also Dr.K.Senga of Keio University for helpful suggestion.

REFERENCE AND NOTES

1 K.Nagahara, K.Takagi, and T.Ueda, Chem. Pharm. Bull. (Tokyo)., 1975, **23**, 3178.

2 The structures of (II) were cofirmed by the spectral data and elemental analyses.

3 The compounds (IIIa-g) were identical in their TLC with the authentic samples prepared by the reported procedure.[1]

4 For example, the spectral data for compound (IIa) are as follows. MS(m/e); 279(M^+), $IR\nu_{max}^{KBr}cm^{-1}$; 1690(C=O), 1630(C=N), 1600(C=C), $UV\lambda_{max}^{EtOH}$nm(logε); 286(3.47), 295(3.50), 307(3.60), 318(3.50), NMR(DMSO-d_6): 2.30(3H, s, C-CH_3), 7.30-8.29(9H, m, aromatic), 12.35 (1H, s, N-OH).

5 The compounds (IIIc,e,f,g) were identical with the authentic samples prepared by the pyrolysis of compounds (Ic,e,f,g).

Received, 8th November, 1978