RESEARCH IN THE IMIDAZOLE SERIES LXXXI.* SYNTHESIS OF 1,4-DIHYDRO DERIVATIVES OF 1,2,4-TRIAZINO[3,4-*a*]BENZIMIDAZOLE

M. V. Povstyanoi, E. V. Logachev, and P. M. Kochergin

UDC 547.785.5'873.07

1,4-Dihydro derivatives of the new 1,2,4-triazino[3,4-a] benzimidazole heterocyclic system were synthesized by reaction of 1-acylmethyl-2-chlorobenzimidazoles with hydrazines.

The reaction of 1-acylmethyl-2-chlorobenzimidazoles (I-VI) with ammonia, primary amines, and thiourea, as a result of which derivatives of imidazo[1,2-a]benzimidazole[2, 3] and thiazolo[3,2-a]benzimidazole [4] were synthesized, has been previously investigated.

In the present research we made a detailed study of the reaction of 1-acylmethyl-2-chlorobenzimidazoles with hydrazine hydrate and alkyl (aryl, hetaryl)hydrazines. As one should have expected, in analogy with the reactions of 3-acylmethyl-2-chloronaphth[1,2-d]imidazoles with hydrazines [5], I-VI react very readily with hydrazine to give, regardless of the ketone residue and the nature of the hydrazine, 1,4-dihydro derivatives of the new 1,2,4-triazino[3,4-*a*]benzimidazole heterocyclic system (VII-XXIII, Table 1).

The reaction proceeds through the formation of the corresponding 1-acylmethyl-2-chlorobenzimidazole hydrazones, which readily split out a molecule of hydrogen chloride under the reaction conditions to give three-ring compounds. When we carried out the reaction of II and III with phenylhydrazine in dioxane at room temperature we were able to isolate intermediate hydrazones XXIV and XXV. The latter withstand brief heating in low-boiling neutral organic solvents but are readily converted to triazinobenzimidazoles XVIII and XIX, respectively, on heating in high-boiling solvents and also in the presence of hydrogen chloride acceptors (triethylamine and pyridine).



The absorption bands of the CO group that are present in the spectra of starting I-VI are absent in the IR spectra of VII-XXIII, whereas the bands of stretching vibrations of the NH group appear at 3150-3300 cm⁻¹ in the spectra of VII-XII. The chemical shifts at 4.50-5.35 ppm in the PMR spectra of VII-XXIII are affiliated with the methylene protons, whereas the group of signals in the aromatic region belong to the protons of the benzene ring (7.00-7.25 ppm) and the phenyl group attached to C_3 (7.40-7.90 ppm); the latter are split into a group of bands with a distance of 0.35-0.5 ppm between the centers, and this constitututes evidence for location of the phenyl group in the α position relative to the tertiary nitrogen atom [6].

*See [1] for communication LXXX.

Kherson Branch, M. V. Lomonosov Odessa Technological Institute of the Food Industry. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1287-1289, September, 1975. Original article submitted Octover 28, 1974.

©1976 Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$15.00.

- p	R	R'	mp, °C (dec.)	Empirical formula	Found, %			Calc., %			Yield,
Con					с	н	N	с	н	N	%
VII VIII VIII VIII XXI XXI XXII XVII XV	$\begin{array}{c} CH_{3} \\ C_{8}H_{5} \\ p-CH_{3}C_{6}H_{4} \\ p-CH_{3}OC_{6}H_{4} \\ p-BrC_{6}H_{4} \\ C_{4}H_{3}S^{b} \\ CH_{3} \\ C_{6}H_{5} \\ p-CH_{3}C_{6}H_{4} \\ p-CH_{3}C_{6}H_{4} \\ C_{4}H_{3}S^{b} \\ C_{6}H_{5} \\ p-CH_{3}C_{6}H_{4} \\ p-CH_{3}OC_{6}H_{4} \\ p-CH_{3}OC_{6}H_{4} \\ c_{6}H_{5} \\ C_{6}H_{5} \\ C_{6}H_{5} \\ C_{6}H_{5} \end{array}$	H H H H CH ₃ CH ₃ CH ₃ C ₃ H ₇ C ₃ H ₇ C ₆ H ₅ C ₆ H ₆ C ₆ H ₆ C	$\begin{array}{c} 293-295\\ 305-308\\ 314-316\\ 286-288\\ 317-319\\ 310-311\\ 127-128\\ 166-168\\ 216-217\\ 167-168\\ 191-192\\ 228-230\\ 230-232\\ 202-204\\ 220-221\\ 220-221\\ 220-221\\ 227-228\\ \end{array}$	$\begin{array}{c} C_{10}H_{10}N_4\\ C_{15}H_{22}N_4\\ C_{16}H_{14}N_4\\ C_{16}H_{14}N_4O\\ C_{16}H_{14}N_4O\\ C_{15}H_{11}N_4B_1^{23}\\ C_{13}H_{10}N_4S\\ C_{11}H_{12}N_4\\ C_{16}H_{14}N_4\\ C_{16}H_{16}N_4\\ C_{19}H_{20}N_4\\ C_{16}H_{16}N_4\\ C_{19}H_{16}N_4\\ C_{22}H_{16}N_4\\ C_{22}H_{18}N_4\\ C_{22$	64,4 72,3 73,3 68,9 54,8 61,6 65,7 72,6 73,6 75,1 65,0 78,1 78,3 74,2 77,9 78,6	5,6 4,7 5,2 5,1 3,2 5,1 5,6 5,3 4,9 5,4 5,4 5,5 4,9 5,4 5,5 5,5 4,9 5,5	30,4 22,8 21,5 19,9 16,8 21,8 21,8 21,4 	64,5 72,6 73,3 69,0 55,1 61,4 65,9 73,2 73,9 75,0 64,8 77,7 78,1 74,5 78,1 78,1 78,1	5,4 4,9 5,4 5,1 3,4 6,0 5,4 5,8 6,6 5,4 5,4 5,4 5,4 5,4 5,4 5,4 5,4 5,4 5,4	30,1 22,5 21,4 20,1 17,1 22,0 27,9 21,4 	$\begin{array}{c} 57\\ 65\\ 85\\ 83\\ 90\\ 60\\ 53\\ 77-80\\ 65-69\\ 80\\ 67\\ 47\\ 57\\ 60\\ 43\\ 67\end{array}$
XXIII	C ₆ H ₅	C₅H₄Nd	198—199	$C_{20}H_{15}N_5$	73,9	4,7	21,7	73,8	4,6	21,6	53

TABLE 1. 1,4-Dihydro-1,2,4-triazino[3,4-*a*]benzimidazole Derivatives (VII-XXIII)

^aFound: Br 24.6%. Calculated: Br 24.4%. ^bThe C₄H₃S grouping is 2-thienyl. ^cFound: S 12.5%. Calculated: S 12.6%. ^dThe C₅H₄N group-ing is 2-pyridyl.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-10 spectrometer. The PMR spectra of trifluoroacetic acid solutions were recorded with a Varian A-60A spectrometer with hexamethyldisiloxane as the internal standard.

1-Acetonyl-2-chlorobenzimidazole (I), 1-phenacyl(p-methyl-, p-methoxy-, p-bromophenacyl)-2-chlorobenzimidazole (II-V) and 1-acetothienyl-2-chlorobenzimidazole (VI) were prepared by known methods [3, 4].

<u>1,4-Dihydro-1,2,4-triazino[3,4-a]benzimidazoles (VII-XXIII, Table 1).</u> A) A solution of 0.01 mole of I-VI and 0.02-0.025 mole of 85% hydrazone hydrate or alkyl(aryl, hetaryl)hydrazine in 20-30 ml of solvent was refluxed for several hours [in dimethylformamide (DMF) for 1-2 h in the preparation of IX, XII, and XIV-XXI, in butanol for 2-3 h in the preparation of VII, VIII, and X-XII, or in ethanol for 4-5 h in the preparation of VII, IX, and XI], after which it was cooled, and the resulting precipitate was removed by filtration and washed with water and cold methanol. The mother liquors were evaporated to a small volume and, in the case of DMF, were poured into water to isolate an additional amount of product. Compounds VII and XVIII were also isolated in 57 and 47% yields, respectively, when the reaction was carried out in methanol or ethanol at 15-18° for 3-4 days.

B) A 0.03-mole sample of methylhydrazine sulfate or o- or p-tolyl hydrazine hydrochloride was added to a solution of 1.2 g (0.03 mole) of NaOH in 10 ml of water and 25-30 ml of DMF, after which the mixture was stirred for 3-5 min. A 0.01-mole sample of I-III was then added, and the mixture was refluxed for 2-3 h. It was then cooled and poured into water, and the precipitate was removed by filtration to give XIII-XV, XXI, and XXII.

C) A mixture of 0.01 mole of 1-acetonyl(phenacyl)-2-chlorobenzimidazole (I, II) and 0.03-0.05 mole of 85% hydrazine hydrate or phenylhydrazine was heated until it solidified, after which it was cooled and washed with water and aqueous alcohol to give VII, VIII, and XVIII in 67, 75, and 53% yields, respectively. No melting-point depressions were observed for mixtures of samples of VII, VIII, and XVIII obtained by the various methods.

Compounds VII-XXIII were colorless or yellow (XII and XIII-XX) crystalline substances of basic character and had blue-green fluorescence of varying intensity in polar solvents. The compounds were purified for analysis by crystallization from aqueous DMF (VII-XII and XVIII-XX), aqueous methanol (XIII, XIV, and XVI), aqueous dioxane (XV and XXIII), or aqueous acetone (XV). IR spectra, NH, cm⁻¹, VII 3176, 3215, and 3300; VIII 3210 and 3290; XI 3150 and 3360; XII 3180 and 3300.

<u>Hydrazones XXIV and XXV.</u> A 1-ml (0.01 mole) sample of phenylhydrazine was added to a solution of 0.005 mole of II or III in 30 ml of dioxane, and the mixture was held at room temperature for 1 week. The resulting precipitate was removed by filtration and washed with ether to give 0.72 g (20%) of brown needles of XXIV with mp 138-140° (from alcohol). Found: N 15.6%. $C_{21}H_{17}ClN_4$. Calculated: N 15.5%. The yield of XXV, with mp 190-192° (dec., from alcohol), was 0.8 g (20%). Found: N 15.0%. $C_{22}H_{19}ClN_4$. Calculated: N 14.9%.

LITERATURE CITED

- 1. V. S. Ponomar', P. M. Kochergin, O. S. Anisimova, Yu. N. Sheinker, B. A. Priimenko, and M. V. Povstyanoi, Khim. Geterotsikl. Soedin., 1284 (1975).
- 2. P. M. Kochergin and V. S. Ponomar', USSR Author's Certificate No. 230,827; Byul. Izobr., No. 35, 22 (1968).
- 3. V. S. Ponomar' and P. M. Kochergin, Khim. Geterotsikl. Soedin., 253 (1972).
- 4. A. N. Krasovskii, P. M. Kochergin, and L. V. Samoilenko, Khim. Geterotsikl. Soedin., 827 (1970).
- 5. P. M. Kochergin and M. V. Povstyanoi, Khim. Geterotsikl. Soedin., 573 (1970).
- 6. A. Le Berre and C. Renault, Bull. Soc. Chim. France, 3139 (1969).