Synthesis of N-Benzyl-(4-amino-3,5-dichloro)-benzoic Acid Hydrazides

By R. S. VARMA*)

Abstract

A series of N-benzyl-(4-amino-3,5-dichloro)-benzoic acid hydrazides have been synthesised as potential monoamine oxidase inhibitors.

Hydrazine derivatives are well known as monoamine oxidase inhibitors, and inhibitors of monoamine oxidase have been reported to possess pronounced anticonvulsant activity[1]). This led the present author to synthesis hitherto unknown hydrazine derivatives of 4-amino-3,5-dichlorobenzoic acid, amides of which have already been shown to possess remarkable anticonvulsant properties[2]).

N-Benzyl-(4-amino-3,5-dichloro)-benzoic acid hydrazides were prepared by reducing corresponding N-benzylidene hydrazine derivatives (synthesised earlier by the present author)[3]) with sodium borohydride. This reagent specifically reduced the $-CONHN{=}CH-$ group to $-CONHNHCH_2-$, and did not affect the other reducible groups present.

Experimental[4])[5])[6])

To a refluxing solution (or suspension) of appropriate N-benzylidene hydrazine (0.01 mole) in 50 ml. of absolute ethanol was added a solution of sodium borohydride (0.02 mole) in 25 ml. of absolute methanol in small portions with vigorous shaking. The reduction was followed by change in the colour of the reaction mixture. The reaction mixture was refluxed for 3—4 hr. Exess solvent was distilled off and water was added. The product was crystallised from a mixture (1:1) of dimethylformamide and 95% ethanol. Melting points, analyses, etc., are recorded in Table 1.

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[1]) J. P. DARWIN, A. SHORE and B. B. BRODIE, Ann. N.Y. Acad. Sci. **80**, 643 (1959).

[2]) B. W. HORROM and T. E. LYNES, J. Med. Chem. **6**, 528 (1963).

[3]) R. S. VARMA, Indian J. Chem. **3**, 233 (1965).

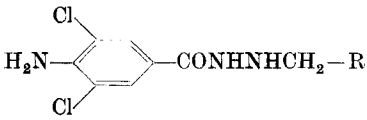
[4]) Melting points were taken in open capillary tubes and are uncorrected.

[5]) Microanalyses were done by SRI ZULFIQAR AHMED of our laboratory.

[6]) Infrared spectra were taken in plates on a Perkin Elmer model 221 spectrophotometer.

Table 1

N-Benzyl-(4-amino-3,5-dichloro)-benzoic acid hydrazides



S.No.		M.P. °C	Yield %	Mol. formula	Chlorine % Found	Calc.
1	Phenyl	238	80	$C_{14}H_{13}Cl_2N_3O$	23.26	22.90
2	2-Hydroxyphenyl[a])	258—260	65	$C_{14}H_{13}Cl_2N_3O_2$	22.04	21.77
3	3-Hydroxyphenyl	221	95	$C_{14}H_{13}Cl_2N_3O_2$	21.98	21.77
4	4-Hydroxyphenyl (decompose)	290	90	$C_{14}H_{13}Cl_2N_3O_2$	22.14	21.77
5	2-Methoxyphenyl	205	75	$C_{15}H_{15}Cl_2N_3O_2$	20.64	20.88
6	3-Methoxyphenyl	196—199	95	$C_{15}H_{15}Cl_2N_3O_2$	20.52	20.88
7	4-Methoxyphenyl	232—233	85	$C_{15}H_{15}Cl_2N_3O_2$	21.31	20.88
8	3,4-Dimethoxyphenyl	235	70	$C_{16}H_{17}Cl_2N_3O_3$	19.33	19.18
9	2-Hydroxy-3-methoxy-phenyl	221—223	60	$C_{15}H_{15}Cl_2N_3O_3$	20.16	19.94
10	2-Chlorophenyl	259—260	75	$C_{14}H_{12}Cl_3N_3O$	30.58	30.91
11	3-Chlorophenyl[b])	205—206	90	$C_{14}H_{12}Cl_3N_3O$	31.28	30.91
12	4-Chlorophenyl	212—213	85	$C_{14}H_{12}Cl_3N_3O$	30.73	30.91
13	3,4-Dioxymethylenephenyl	224—225	90	$C_{15}H_{13}Cl_2N_3O_3$	19.51	20.05
14	4-Diethylaminephenyl[c])	258	85	$C_{18}H_{22}Cl_2N_4O$	19.08	18.63
15	2-Furyl	200	85	$C_{12}H_{11}Cl_2N_3O_2$	23.96	23.66

Infrared absorption peaks [a]) cm^{-1} 3480, 3380 (OH, NH_2, NH), 1600 (—CONH); [b]) cm^{-1} 3480, 3380 (NH_2, NH), 1595 (—CONH); [c]) cm^{-1} 3500, 3395 (NH_2, NH), 1595 (—CONH).

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