

SYNTHESIS OF SOME NEW 3-HETEROCYCLYL-1,2,3-BENZOTRIAZIN-4(3H)-ONES

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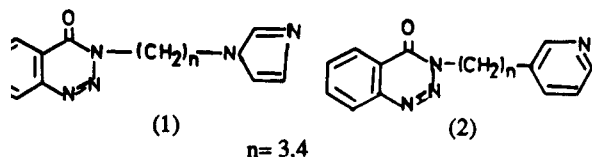
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Abstract

Some new 3-heterocyclyl-1,2,3-benzotriazin-4(3H)-ones (7a-f) were prepared in moderate to good yields by nitrosation of N-heterocyclyl-2-aminobenzanilides (6a-f). The latter were obtained by hydrazine hydrate-graphite reduction of corresponding N-heterocyclyl-2-nitrobenzanilides (5a-f).

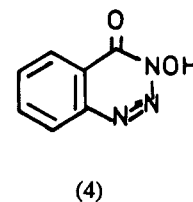
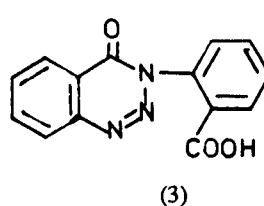
Introduction

A large number of 3-alkyl, 3-aryl and 3-azalkyl-1,2,3-benzotriazin-4(3H)-ones have been prepared and their thermolytic [1] and photolytic [2,3] decompositions and degradations [4] have been studied extensively. 1,2,3-Benzotriazinone or its 3-aryl derivatives undergo decomposition [5] with sodium azide or sodium iodide in boiling acetic acid to afford 2-azido and 2-iodobenzamides respectively in high yields. Thermolysis of nuclear substituted benzotriazinones in an inert solvent have been reported to yield 2-(o-tolylphenyl)-3,1-benzoxazin-4-ones [6,7]. However, relatively few 3-heterocyclyl derivatives have been so far prepared and studied.



3-Heteroaryl-1,2,3-benzotriazin-4-(3H)-ones such as 3-(1-imidazolylalkyl)-4(3H)-ones (1), 3-(2-pyridinylalkyl)- or 3-(pyridinyl alkyl)-1,2,3-benzotriazin-4(3H)-ones (2) are cardiovascular agents and are antithrombotics [8,9]. They are useful in treating ischemia, thrombosis, hypertension and migraine. 3-benzotriazinyl benzoate e.g. (3) are plant growth regulators and agrochemical fungicides [10].

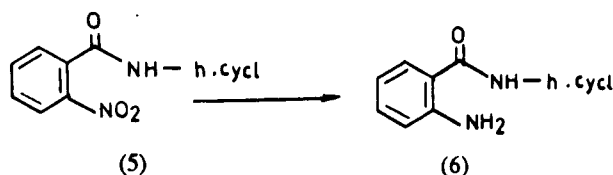
Keywords: Aminobenzanilide; Benzotriazin; Nitrosation



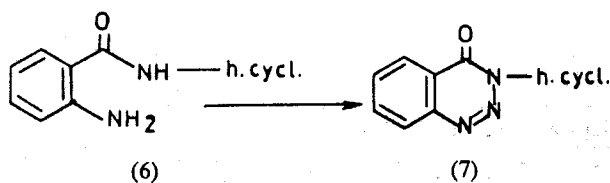
3-Hydroxybenzotriazin-4-ones (4) have been reported [11] to be self indicating effective acylating agents in solid-phase peptide synthesis.

Results

2-Nitro-N-heterocyclylbenzanilides (5) were prepared by reaction of 2-nitrobenzoyl chloride with heterocyclyl amines in dry pyridine during preparation of 2-heterocyclyl-1,2-dihydro-3H-indazol-3-ones as reported earlier [12]. Table 1 gives the physical data for some of these compounds (5).



These nitrobenzanilides (5) were reduced to corresponding 2-amino-anilides (6) using hydrazine hydrate-graphite method [13]. Other attempted reduction methods using zinc-HCl or stannous chloride-HCl failed.



The amino derivatives were characterized by lack of absorptions due to NO_2 stretching at $1524\text{--}1534\text{ cm}^{-1}$ and by the appearance of two sharp distinct peaks at 3430 cm^{-1} and 3340 cm^{-1} due to unsymmetrical and symmetrical -NH_2 stretching respectively. The mass spectra and physical data for N-heterocyclyl-2-aminobenzanilides (6) are summarized in Table 2.

2-Aminobenzanilides are useful compounds which show strong anticonvulsant activity [14]. Diazotization of N-heterocyclyl-2-aminobenzanilides (6) in 2N hydrochloric acid at $0\text{--}5^\circ\text{C}$ followed by basification with aqueous ammonia liberated the 3-heterocyclyl-

1,2,3-benzotriazin-4(3H)-ones (7). Their physical data is listed in Table 3.

Experimental Section

Melting points were determined using MEL-TEMP MP-D apparatus and are uncorrected. IR spectra were recorded on a Hitachi spectrophotometer Model-270 as KBr discs or as neat liquids. E.I.M.S. were recorded on a Mat-112-S machine at 70 eV.

Reduction of N-heterocyclyl-2-nitrobenzanilides (5a-f) to N-heterocyclyl-2-aminobenzanilides (6a-f) General Procedure

A mixture of N-heterocyclyl-2-nitrobenzanilides (5a-f) (0.01 mol), hydrazine hydrate (0.02 mol) graphite (3 g) was refluxed for 2-3 hours under atmospheric pressure of nitrogen. The reaction mixture was filtered and washed with ethanol to remove graphite. Removal of solvents by flash evaporation af-

Table 1. 2-Nitro-N-heterocyclylbenzomilides (5)

(5)	Heterocyclyl	M.P.($^\circ\text{C}$)	Yield(%)	Recryst. Solvent(s)
a	2,5-thiazolyl	243-245	64.5	DMF-ethanol
b	1-(8-quinolinyl)	195-196	80.5	Ethyl acetate
c	3-pyridylmethyl	120-122	51.5	Ethyl acetate
d	2-pyridyl	135-137	57.6	DMF- H_2O
e	4-pyridyl	216-218	52.5	DMF- H_2O
f	p-(N, N-diethyl-aminophenyl)	21	72.0	Ethanol

Table 2. N-Heterocyclyl-2-aminobenzanilides (6)

(6)	Heterocyclyl	M.P.($^\circ\text{C}$)	Yield	M.S. (m/z)
a	2,5-thiazolyl	152-153	60	204
b	1-(8-quinolinyl)	137-138	69	218
c	3-pyridylmethyl	112-114	45	212
d	2-pyridyl	176-180	40	198
e	4-pyridyl	193-194	29	198
f	p-(N, N-diethyl-aminophenyl)	126-128	82	268

Table 3. 3-Heterocyclyl-1,2,3-benzotriazin-4(3H)-ones (7)

(7)	M.P.($^\circ\text{C}$)	Yield (5)	M.S. (m/z)
a	172-174	54	230
b	196-198	69	244
c	162-164	45	238
d	195-196	40	224
e	254-256	29	224
f	77-79	46	294

forded N-heterocyclyl-2-aminobenzanilides (6a-f) which were recrystallized from aqueous ethanol.

3-(3-Pyridylmethyl)-1,2,3-benzotriazin-4(3H)-one (7c)

Typical Procedure

To a stirred solution of N-(3-pyridylmethyl)-2-aminobenzanilide (6c) (0.6 g, 0.0026 mol) in 2N hydrochloric acid (5.5 ml) was diazotized with a solution of sodium nitrite (0.23 g, 0.0035 mol) in water (3 ml) at 0°C. Basification with aqueous ammonia yielded 3-(3-pyridylmethyl)-1,2,3-benzotriazin-4-(3H)-one (7c) (0.28 g, 0.0012 mol, 45%) m.p. 162-164°C.

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